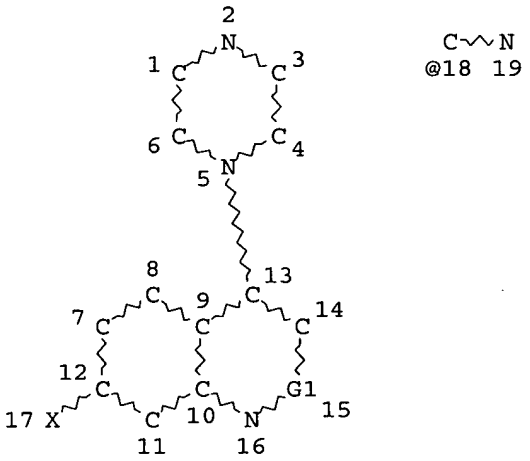
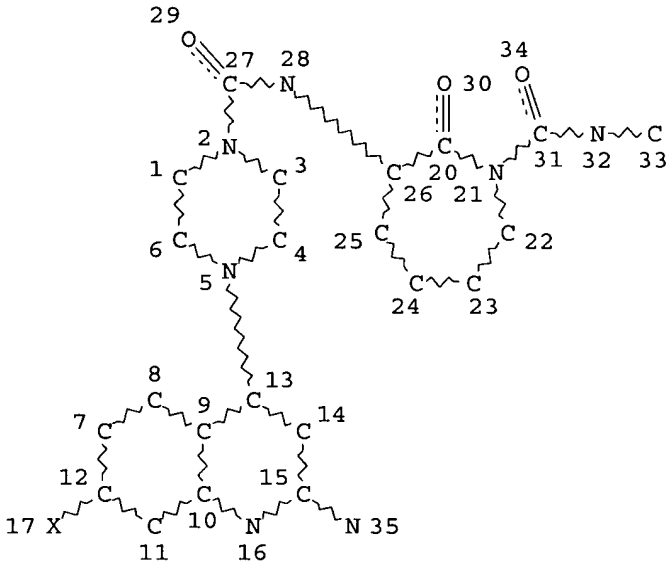
```
=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 20:43:23 ON 10 SEP 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)
```



```
FILE COVERS 1907 - 10 Sep 2005  VOL 143 ISS 12
FILE LAST UPDATED: 9 Sep 2005  (20050909/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=>
=>

=> d stat que
L66              STR
```




```
VAR G1=CH/18
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  19

STEREO ATTRIBUTES: NONE
L68          601 SEA FILE=REGISTRY SSS FUL L66
L69              STR
```



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 33

STEREO ATTRIBUTES: NONE
L70 12 SEA FILE=REGISTRY SUB=L68 SSS FUL L69
L71 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L70

=>
=>

=> d ibib abs hitstr l71 1

L71 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:20661 HCAPLUS
DOCUMENT NUMBER: 140:93938
TITLE: Preparation of substituted quinolines useful as CCR5 receptor antagonists
INVENTOR(S): Dunning, Laura; Jaroch, Stefan; Kochanny, Monica J.; Lee, Wheeseong; Lian, Xiongdong; Liang, Meina; Lu, Shou-Fu; Onuffer, James; Phillips, Gary; Wei, Guo-Ping; Ye, Bin
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 241 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004002960	A1	20040108	WO 2003-US20950	20030624

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2489560	AA	20040108	CA 2003-2489560		20030624
BR 2003012204	A	20050426	BR 2003-12204		20030624
EP 1534681	A1	20050601	EP 2003-762325		20030624

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

US 2004072818	A1	20040415	US 2003-607530		20030626
PRIORITY APPLN. INFO.:			US 2002-451687P	P	20020627
			WO 2003-US20950	W	20030624

OTHER SOURCE(S): MARPAT 140:93938
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

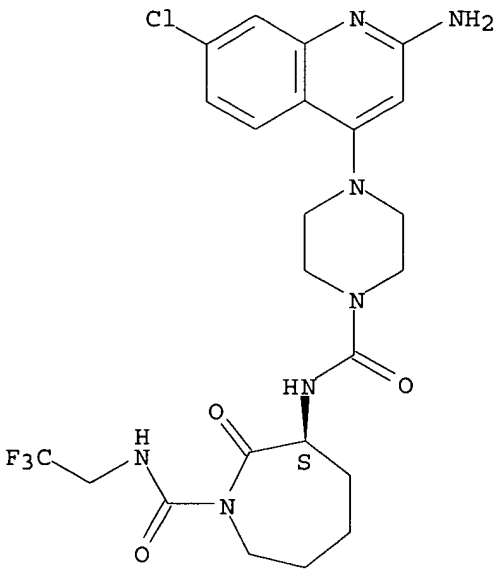
AB The present invention relates to quinoline derivs. of formula I and II [wherein: R1, R1* = H, (un)substituted amino, alkyl, haloalkyl, OH, alkoxy, CO2R9a; R2, R2*, R3, R3* = H, (halo)alkyl, halogen, (un)substituted amino, nitro, cyano, alkoxy; R4, R4* = H, alkyl; R5 = H, R9, R9-aminocycloalk(en)yl, (alk/aryl)oxycarbonyl, SO2R9, C(O)NR7R9, C(O)NR7-SO2R9, C(O)R6, C(O)R9, C(=NR10)R9, C(S)R9, C(=NR10)NHR9, C(S)NHR9, C(S)NR7-SO2R9; R6 is a group of formula III; R7, R7* = H, (un)substituted alkyl or aryl; R9a = arylalkyl, cycloalk(en)yl, cycloalkylalkyl, alkyl, heterocyclylalkyl, aryl, heterocyclyl any of which can be (un)substituted; R9 is same as R9a except H; R10 = H, cyano, (un)substituted alkyl or alkoxy; n = 0-3, n* = 1-3], their enantiomers, diastereomers, salts, and solvates. For instance, quinoline IV was prepared via amination of 4,7-dichloroquinoline by piperazine, and subsequent addition of obtained 7-chloro-4-(piperazin-1-yl)quinoline to 4-FC6H4NCO. The invention compds. are claimed as CCR5 receptor antagonists (no data) and useful for treating the CCR5-mediated inflammatory and immunoregulatory disorders such as optic neuritis, stroke, dermatitis, HIV, diabetes, etc.

IT **643047-25-0P 643047-34-1P 643047-58-9P**
643047-69-2P 643047-71-6P 643047-73-8P
643047-79-4P 643047-83-0P 643048-21-9P
643048-26-4P 643048-31-1P 643048-36-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinoline derivs. useful as CCR5 receptor antagonists)

RN 643047-25-0 HCAPLUS

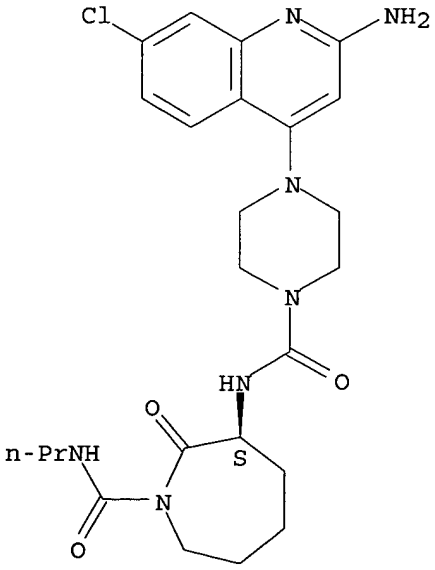
CN 1H-Azepine-1-carboxamide, 3-[[[4-(2-amino-7-chloro-4-quinolinyl)-1-piperazinyl]carbonyl]amino]hexahydro-2-oxo-N-(2,2,2-trifluoroethyl)-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



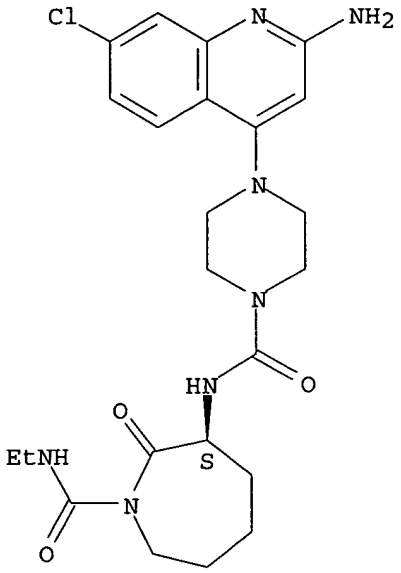
RN 643047-34-1 HCAPLUS
CN 1H-Azepine-1-carboxamide, 3-[[[4-(2-amino-7-chloro-4-quinolinyl)-1-piperazinyl]carbonyl]amino]hexahydro-2-oxo-N-propyl-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



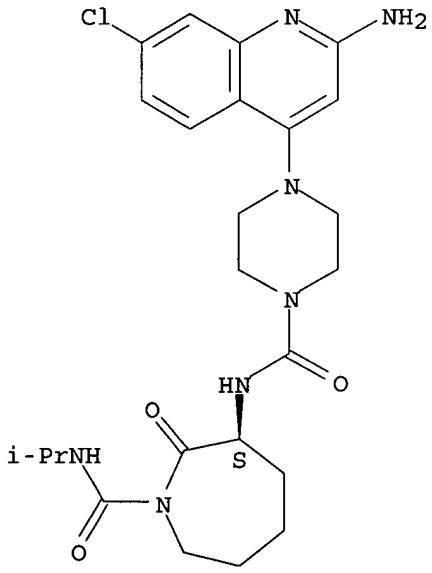
RN 643047-58-9 HCAPLUS
CN 1H-Azepine-1-carboxamide, 3-[[[4-(2-amino-7-chloro-4-quinolinyl)-1-piperazinyl]carbonyl]amino]-N-ethylhexahydro-2-oxo-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



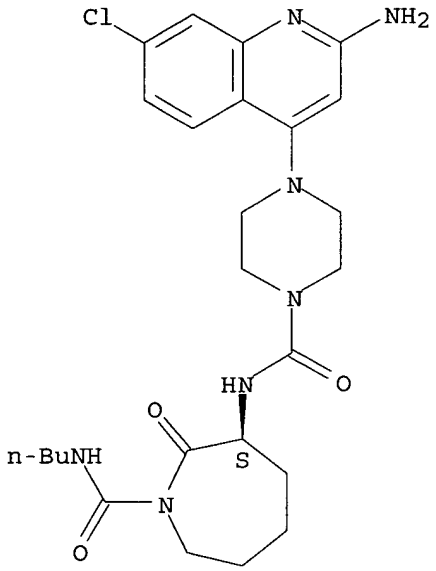
RN 643047-69-2 HCAPLUS
CN 1H-Azepine-1-carboxamide, 3-[[[4-(2-amino-7-chloro-4-quinolinyl)-1-piperazinyl]carbonyl]amino]hexahydro-N-(1-methylethyl)-2-oxo-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



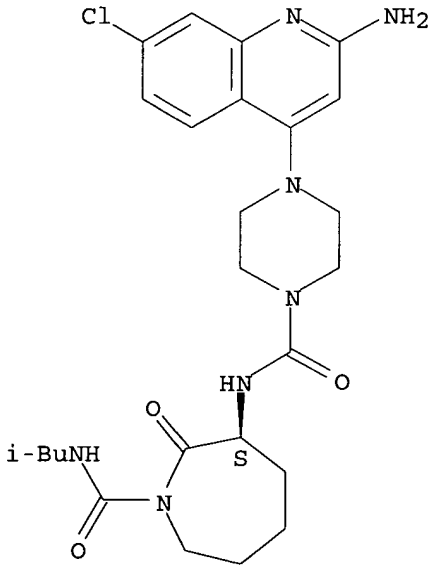
RN 643047-71-6 HCAPLUS
CN 1H-Azepine-1-carboxamide, 3-[[[4-(2-amino-7-chloro-4-quinolinyl)-1-piperazinyl]carbonyl]amino]-N-butylhexahydro-2-oxo-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



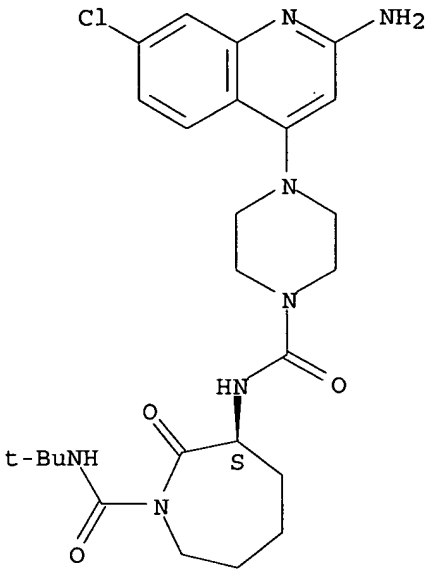
RN 643047-73-8 HCAPLUS
CN 1H-Azepine-1-carboxamide, 3-[[[4-(2-amino-7-chloro-4-quinolinyl)-1-piperazinyl]carbonyl]amino]hexahydro-N-(2-methylpropyl)-2-oxo-, (3S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



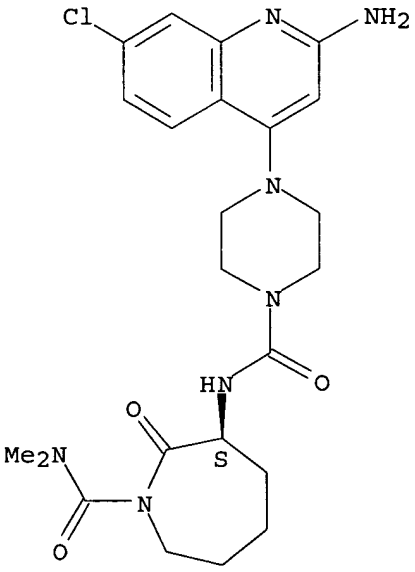
RN 643047-79-4 HCAPLUS
CN 1H-Azepine-1-carboxamide, 3-[[[4-(2-amino-7-chloro-4-quinolinyl)-1-piperazinyl]carbonyl]amino]-N-(1,1-dimethylethyl)hexahydro-2-oxo-, (3S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



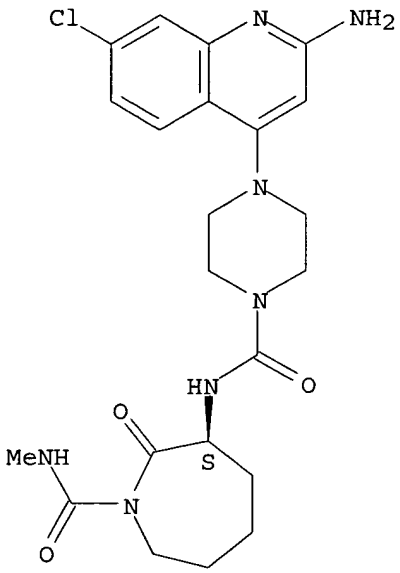
RN 643047-83-0 HCAPLUS
CN 1H-Azepine-1-carboxamide, 3-[[[4-(2-amino-7-chloro-4-quinolinyl)-1-piperazinyl]carbonyl]amino]hexahydro-N,N-dimethyl-2-oxo-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



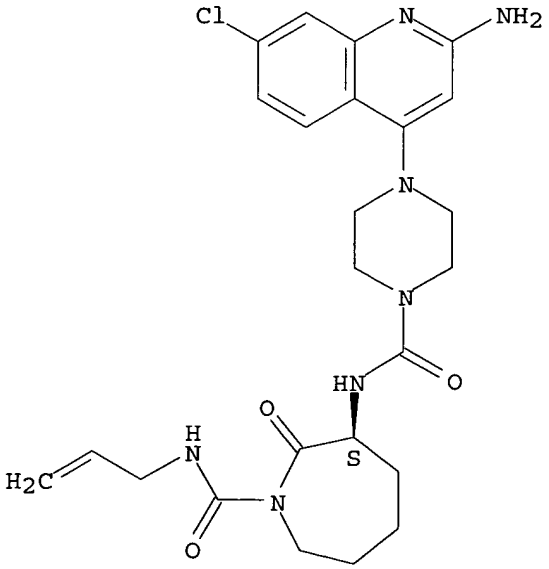
RN 643048-21-9 HCAPLUS
CN 1H-Azepine-1-carboxamide, 3-[[[4-(2-amino-7-chloro-4-quinolinyl)-1-piperazinyl]carbonyl]amino]hexahydro-N-methyl-2-oxo-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



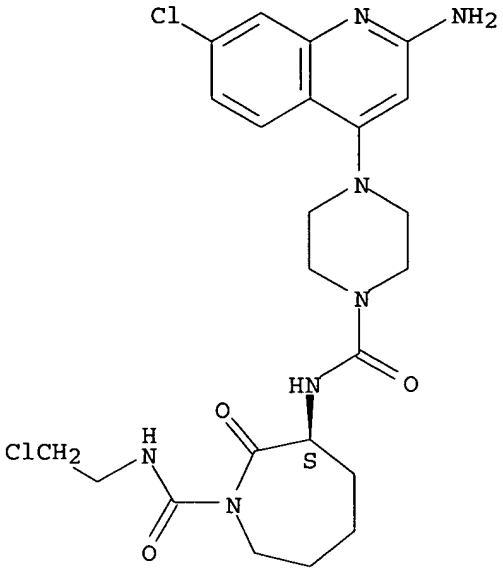
RN 643048-26-4 HCAPLUS
CN 1H-Azepine-1-carboxamide, 3-[[[4-(2-amino-7-chloro-4-quinolinyl)-1-piperazinyl]carbonyl]amino]hexahydro-2-oxo-N-2-propenyl-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



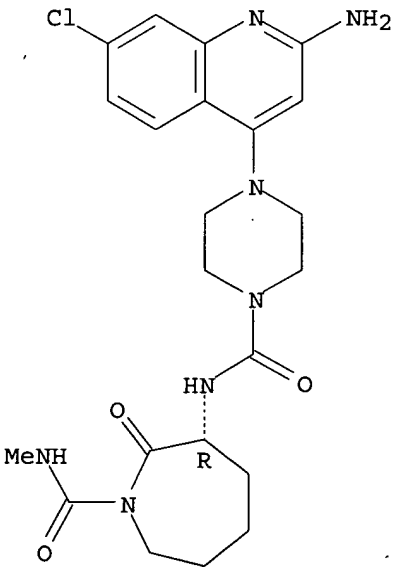
RN 643048-31-1 HCAPLUS
CN 1H-Azepine-1-carboxamide, 3-[[[4-(2-amino-7-chloro-4-quinolinyl)-1-piperazinyl]carbonyl]amino]-N-(2-chloroethyl)hexahydro-2-oxo-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



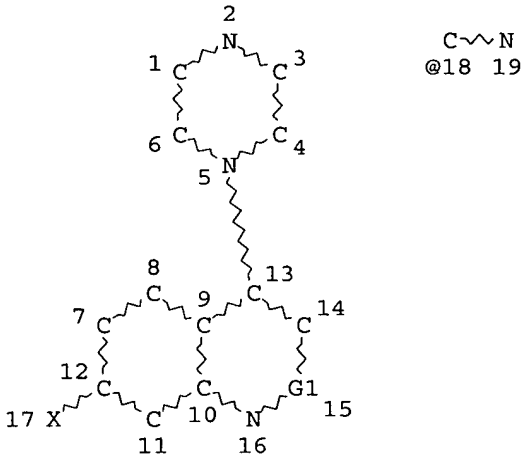
RN 643048-36-6 HCAPLUS
CN 1H-Azepine-1-carboxamide, 3-[[[4-(2-amino-7-chloro-4-quinolinyl)-1-piperazinyl]carbonyl]amino]hexahydro-N-methyl-2-oxo-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

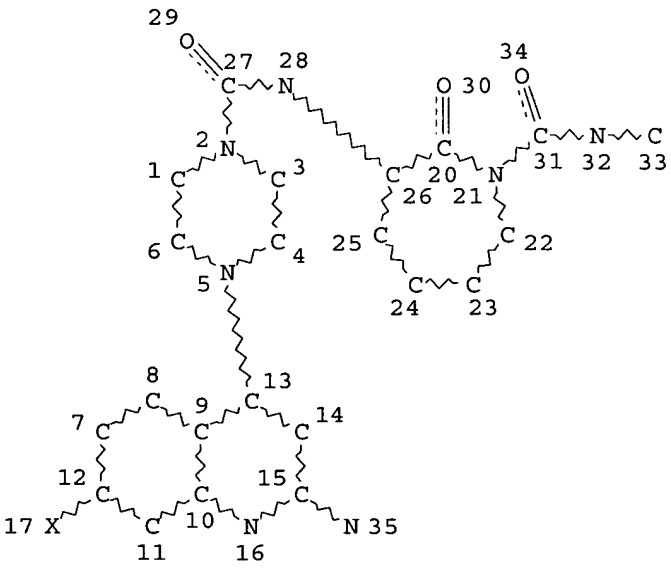
=> => d stat que l76
L66 STR



VAR G1=CH/18
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 19

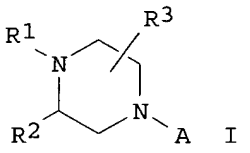
STEREO ATTRIBUTES: NONE
L68 601 SEA FILE=REGISTRY SSS FUL L66
L69 STR



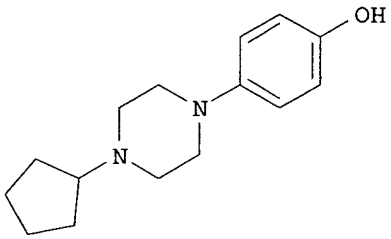
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 33

```
STEREO ATTRIBUTES: NONE
L70          12 SEA FILE=REGISTRY SUB=L68 SSS FUL L69
L71           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L70
L72         589 SEA FILE=REGISTRY ABB=ON  PLU=ON  L68 NOT L70
L73         102 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L72
L74          86 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L73 AND PD=<OCTOBER 24, 2003
L75          86 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L74 NOT L71
L76          20 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L75 AND PATENT/DT


=>
=>

=> d ibib abs hitstr l76 1-20

L76  ANSWER 1 OF 20  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:        2003:633674  HCAPLUS
DOCUMENT NUMBER:         139:180085
TITLE:                   Preparation of novel aryl- and heteroarylpiperazines
                         with histamine H3 receptor affinity
INVENTOR(S):             Hohlweg, Rolf; Doerwald, Florencio Zaragoza;
                         Stephensen, Henrik; Pettersson, Ingrid; Peschke, Bernd
PATENT ASSIGNEE(S):      Novo Nordisk A/S, Den.; Boehringer Ingelheim
                         International G.m.b.H.
SOURCE:                  PCT Int. Appl., 145 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    --------------------     --------
     WO 2003066604         A2    20030814    WO 2003-DK300071         20030205 <--
     WO 2003066604         A3    20031204
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     CA 2474214            AA    20030814    CA 2003-2474214          20030205 <--
     EP 1474401            A2    20041110    EP 2003-701482           20030205
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
     BR 2003007429         A     20041228    BR 2003-7429             20030205
     US 2003236259         A1    20031225    US 2003-383310           20030307
PRIORITY APPLN. INFO.:                       DK 2002-168          A   20020205
                                             US 2002-356630P      P   20020208
                                             DK 2002-1142         A   20020726
                                             US 2002-399304P      P   20020726
                                             WO 2003-DK71         W   20030205
OTHER SOURCE(S):         MARPAT 139:180085
GI
```



I



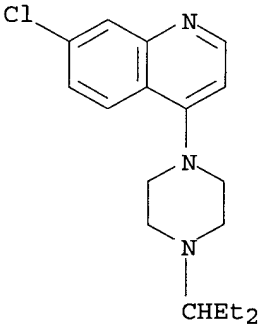
II

AB Novel aryl- and heteroarylpiperazines of formula I [R1 = alkyl, alkenyl, alkynyl, cycloalkyl, not isobutyl; R2 = H, alkyl; R1R2 = alkylene; R3 = H, halo, OH, CF3, OCF3, alkyl, cycloalkyl, alkoxy, aryl, etc.; A = aryl, heteroaryl, etc.] are prepared and used in pharmaceutical compns. The compds. show a high and selective binding affinity to the histamine H3 receptor indicating histamine H3 receptor antagonistic, inverse agonistic or agonistic activity. As a result, the compds. are useful for the treatment of diseases and disorders related to the histamine H3 receptor. Thus, II was prepared from 1-(4-hydroxyphenyl)piperazine and cyclopentanone in 49% yield.

IT **577966-28-0P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aryl- and heteroarylpiperazines with histamine H3 receptor affinity)

RN 577966-28-0 HCAPLUS

CN Quinoline, 7-chloro-4-[4-(1-ethylpropyl)-1-piperazinyl]-, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

L76 ANSWER 2 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:300733 HCAPLUS
DOCUMENT NUMBER: 136:284410
TITLE: Antimalarial dihydroartemisinin formulation
INVENTOR(S): Li, Guoqian
PATENT ASSIGNEE(S): Jianqiao Medicine Development Co., Ltd., Chongqing City, Peop. Rep. China

SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 5 pp.
CODEN: CNXXEV
DOCUMENT TYPE: **Patent**
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1305810	A	20010801	CN 2000-113134	20000823 <--
CN 1135972	B	20040128		
WO 2002026226	A1	20020404	WO 2001-CN884	20010531 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001089506	A5	20020408	AU 2001-89506	20010531 <--

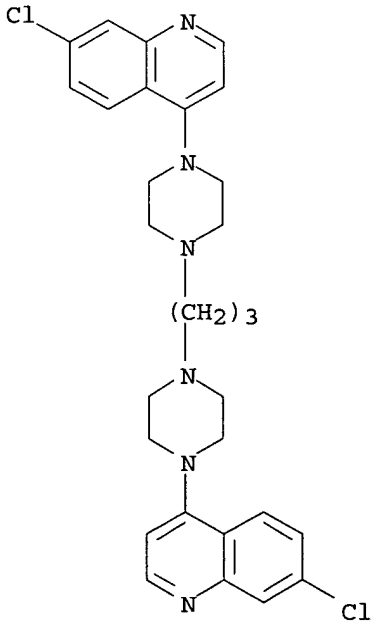
PRIORITY APPLN. INFO.:
CN 2000-113134 A 20000823
WO 2001-CN884 W 20010531

AB An antimalarial preparation (such as tablet, capsule, granule, or injection) is composed of dihydroartemisinin or its analog (such as arteannuin, artesunate, artemether, or arteether) 1, piperaquine or its phosphate 3-7, and trimethoprim 0- 5 part.

IT **4085-31-8**, Piperaquine **85547-56-4**, Quinoline, 4,4'-(1,3-propanediyldi-4,1-piperazinediyl)bis[7-chloro-, phosphate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antimalarial dihydroartemisinin formulation)

RN 4085-31-8 HCAPLUS

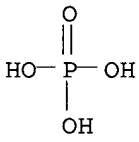
CN Quinoline, 4,4'-(1,3-propanediyldi-4,1-piperazinediyl)bis[7-chloro- (9CI) (CA INDEX NAME)



RN 85547-56-4 HCAPLUS
CN Quinoline, 4,4'-(1,3-propanediyldi-4,1-piperazinediyl)bis[7-chloro-, phosphate (9CI) (CA INDEX NAME)

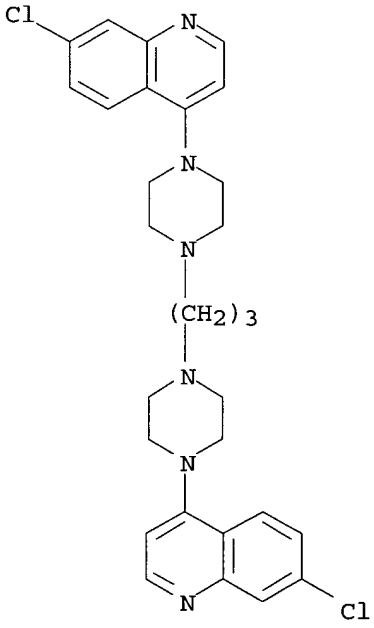
CM 1

CRN 7664-38-2
CMF H3 O4 P



CM 2

CRN 4085-31-8
CMF C29 H32 Cl2 N6

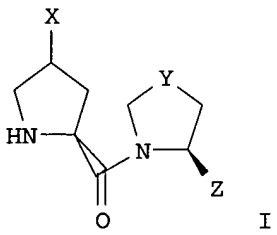


L76 ANSWER 3 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:142666 HCAPLUS
DOCUMENT NUMBER: 136:200479
TITLE: Preparation of proline derivatives as dipeptidyl peptidase IV (DPP-IV) inhibitors and use thereof as drugs
INVENTOR(S): Kitajima, Hiroshi; Sakashita, Hiroshi; Akahoshi, Fumihiko; Hayashi, Yoshiharu
PATENT ASSIGNEE(S): Welfide Corporation, Japan
SOURCE: PCT Int. Appl., 340 pp.

CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
WO 2002014271	A1	20020221	WO 2001-JP6906		20010810	<--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM						
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG						
CA 2418656	AA	20020221	CA 2001-2418656		20010810	<--
AU 2001077754	A5	20020225	AU 2001-77754		20010810	<--
EP 1308439	A1	20030507	EP 2001-955660		20010810	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR						
BR 2001013146	A	20030624	BR 2001-13146		20010810	<--
NZ 524618	A	20040827	NZ 2001-524618		20010810	
NO 2003000619	A	20030226	NO 2003-619		20030207	<--
US 2004106655	A1	20040603	US 2003-344255		20030210	
PRIORITY APPLN. INFO.:			JP 2000-243217	A	20000810	
			JP 2000-400296	A	20001228	
			WO 2001-JP6906	W	20010810	

OTHER SOURCE(S): MARPAT 136:200479
GI



I

AB The title compds. [I; X = NR1R2, NR3COR4, NR5COR4, NR5CH2CH2NR6R7, NR8SO2R9, OR10, O2CR11; wherein R1, R2 = H, alkyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, or they are linked to each other to form a heterocyclyl containing 1 or 2 N atoms or O which may be a spiro ring and is optionally fused to an (un)substituted aromatic ring; R3, R4 = H, alkyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, arylalkenyl, heteroaryl, heteroarylalkyl; R5, R6, R7 = H, alkyl, acyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heteroaryl, or heteroarylalkyl, or which is optionally fused to an (un)substituted aromatic ring; R8, R9, R10, R11 = H, alkyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heteroaryl, or heteroarylalkyl] or pharmacol. acceptable salts thereof are prepared These compds. are useful for the treatment of DPP-IV related diseases such as diabetes, obesity, HIV infection, cancer metastasis, skin diseases, prostatic hypertrophy (prostatomegaly), pericementitis, or autoimmune diseases. Thus, a solution of 0.924 g

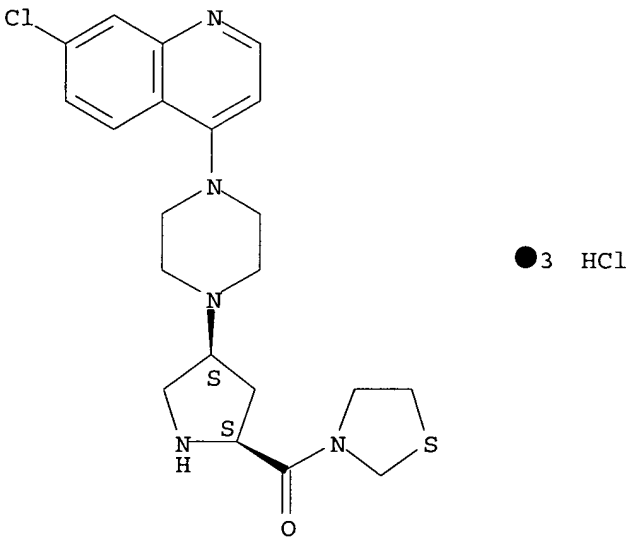
(S)-1-[(2S,4S)-4-amino-1-tert-butoxycarbonyl-2-pyrrolidinylcarbonyl]-2-cyanopyrrolidine (preparation given), 1.7 mL diisopropylethylamine, and 0.78 g 2-chloro-4-fluorobenzonitrile in 10 mL N-methyl-2-pyrrolidone were stirred at 80° for 4 h to give 0.94 g (S)-1-[(2S,4S)-1-tert-butoxycarbonyl-4-(3-chloro-4-cyanophenyl)amino-2-pyrrolidinylcarbonyl]-2-cyanopyrrolidine which (0.93 g) was treated with HCl/EtOAc at room temperature for 15 h to give (S)-1-[(2S,4S)-4-(3-chloro-4-cyanophenyl)amino-2-pyrrolidinylcarbonyl]-2-cyanopyrrolidine hydrochloride (II). II showed IC50 of 0.13 and 0.15 nM against human blood plasma DPP-IV and rat blood plasma DPP-IV, resp.

IT **401563-64-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of proline derivs. as dipeptidyl peptidase IV (DPP-IV) inhibitors for treating DPP-IV related diseases)

RN 401563-64-2 HCAPLUS

CN Thiazolidine, 3-[[(2S,4S)-4-[4-(7-chloro-4-quinolinyl)-1-piperazinyl]-2-pyrrolidinyl]carbonyl]-, trihydrochloride (9CI) (CA INDEX NAME)

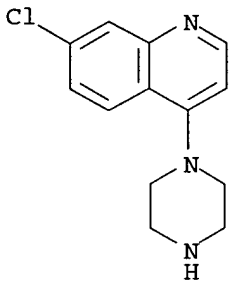
Absolute stereochemistry.



IT **837-52-5P 401567-71-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of proline derivs. as dipeptidyl peptidase IV (DPP-IV) inhibitors for treating DPP-IV related diseases)

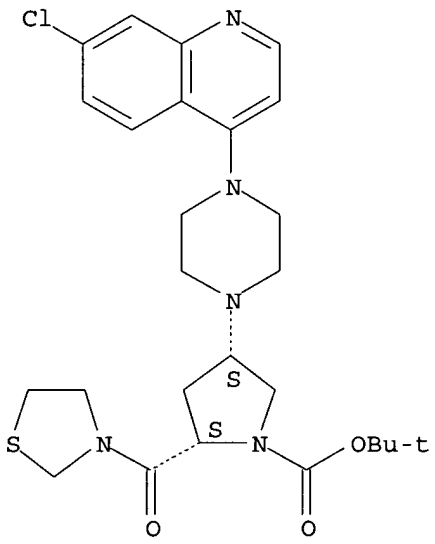
RN 837-52-5 HCAPLUS

CN Quinoline, 7-chloro-4-(1-piperazinyl)- (7CI, 8CI, 9CI) (CA INDEX NAME)



RN 401567-71-3 HCAPLUS
CN 1-Pyrrolidinecarboxylic acid, 4-[4-(7-chloro-4-quinolinyl)-1-piperazinyl]-2-(3-thiazolidinylcarbonyl)-, 1,1-dimethylethyl ester, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

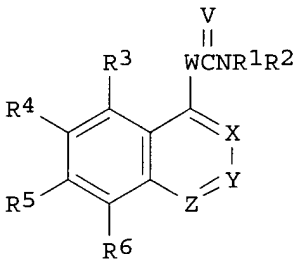
L76 ANSWER 4 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:10086 HCAPLUS
DOCUMENT NUMBER: 134:86277
TITLE: 1,3-Diazines with platelet-derived growth factor receptor inhibitory activity
INVENTOR(S): Matsuno, Kenji; Ichimura, Michio; Nomoto, Yuji; Fujiwara, Shigeki; Ide, Shinichi; Tsukuda, Eiji; Irie, Junko; Oda, Shoji
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: U.S., 127 pp., Cont.-in-part of PCT 9814431.
CODEN: USXXAM
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6169088	B1	20010102	US 1998-88199	19980601 <--
WO 9814431	A1	19980409	WO 1997-JP3510	19971001 <--
W: AU, BG, BR, CA, CN, CZ, HU, JP, KR, MX, NO, NZ, PL, RO, SG, SI, SK, UA, US, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6207667	B1	20010327	US 2000-481544	20000112 <--
US 2002068734	A1	20020606	US 2000-734918	20001213 <--
US 6472391	B2	20021029		

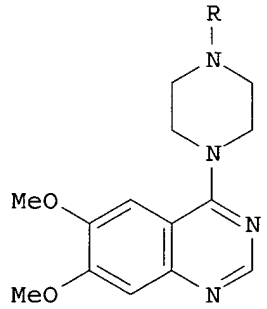
PRIORITY APPLN. INFO.:	JP 1996-260743	A 19960110
	WO 1997-JP3510	A2 19971001
	US 1998-88199	A3 19980601
	US 2000-481544	A3 20000112

OTHER SOURCE(S): MARPAT 134:86277

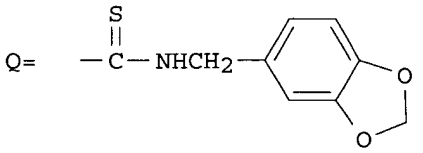
GI



I



II



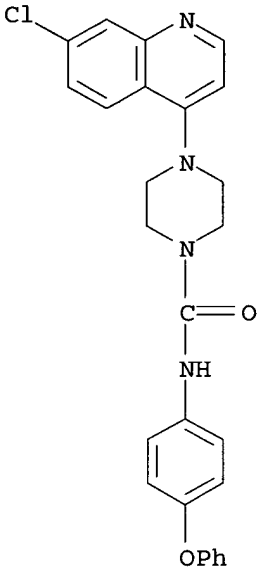
AB 1,3-Diazines and related N heterocycles [I; wherein V = O or S; W = 1,4-piperazinediyl or 1,4-homopiperazinediyl which may be substituted with unsubstituted alkyl on the ring; X = N or CR9; Y = N or CR8; Z = N or CR7, with at least one of X, Y and Z being N; R1 = H, (un)substituted alkyl, cycloalkyl, aryl, heterocyclyl, etc.; R2 = substituted alkyl, (un)substituted cycloalkyl, aryl, heterocyclyl, etc.; R3, R4, R5, R6 = H, halo, (un)substituted alkyl, NO2, cyano, (un)substituted OH or NH2, etc.; R7, R8 = R1 groups, halo, etc.; R9 = H, CO2H or derivs.] and their pharmacol. acceptable salts are prepared These compds. inhibit the phosphorylation of PDGF receptors and the abnormal proliferation or migration of cells, and so are effective in preventing or treating cell proliferative diseases such as arteriosclerosis, vascular reocclusion diseases, cancer, and glomerulosclerosis. Thus, 6,7-dimethoxy-4-(1-piperazinyl)quinazoline reacted with Ph isocyanate in refluxing EtOH to give invention compound II [R = CONHPh] in 44% isolated yield. The analog II [R = Q] showed an IC50 of 0.03 μM for inhibiting the phosphorylation of PDGF receptor in vitro. Pharmaceutical formulations, e.g. tablets containing II [R = N-(p-nitrophenyl)carbamoyl], were prepared

IT **205255-54-5P 205258-54-4P 205258-55-5P**

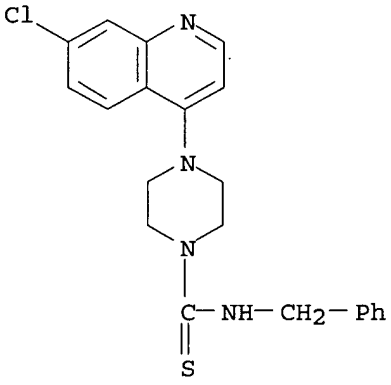
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 1,3-diazines with platelet-derived growth factor receptor inhibitory activity)

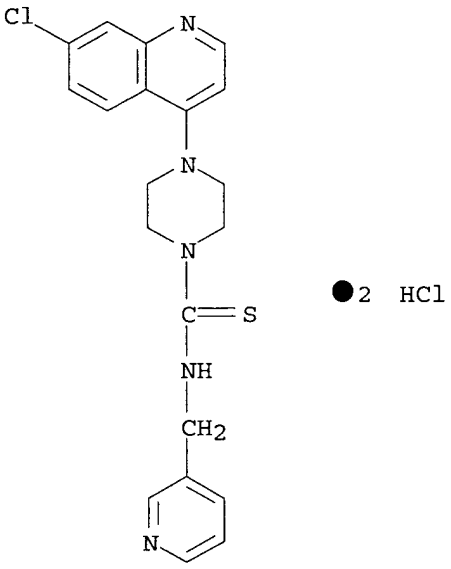
RN 205255-54-5 HCAPLUS
CN 1-Piperazinecarboxamide, 4-(7-chloro-4-quinolinyl)-N-(4-phenoxyphenyl)-(9CI) (CA INDEX NAME)



RN 205258-54-4 HCAPLUS
CN 1-Piperazinecarbothioamide, 4-(7-chloro-4-quinolinyl)-N-(phenylmethyl)-(9CI) (CA INDEX NAME)

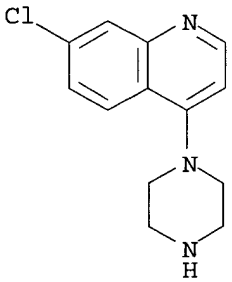


RN 205258-55-5 HCAPLUS
CN 1-Piperazinecarbothioamide, 4-(7-chloro-4-quinolinyl)-N-(3-pyridinylmethyl)-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

IT **837-52-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 1,3-diazines with platelet-derived growth factor receptor inhibitory activity)
RN 837-52-5 HCAPLUS
CN Quinoline, 7-chloro-4-(1-piperazinyl)- (7CI, 8CI, 9CI) (CA INDEX NAME)

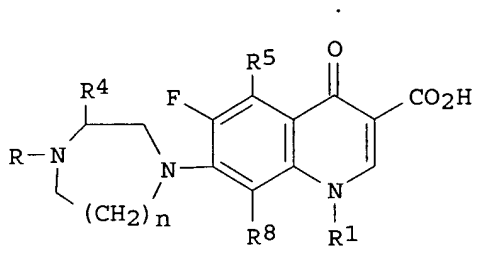


REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

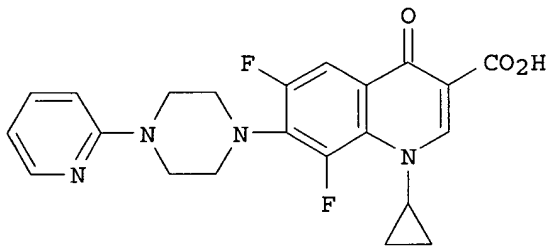
L76 ANSWER 5 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:688628 HCAPLUS
DOCUMENT NUMBER: 133:222588
TITLE: Preparation of carbostyrils and their use as antimycoplasma agents
INVENTOR(S): Yang, Yushe; Ji, Ruyun; Chen, Kaixian
PATENT ASSIGNEE(S): Shanghai Medicine Inst., Chinese Academy of Sciences, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 20 pp.
CODEN: CNXXEV
DOCUMENT TYPE: **Patent**
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1234397	A	19991110	CN 1999-113598	19990402 <--
CN 1091103	B	20020918		
PRIORITY APPLN. INFO.:			CN 1999-113598	19990402
OTHER SOURCE(S):	MARPAT 133:222588			

GI



I



II

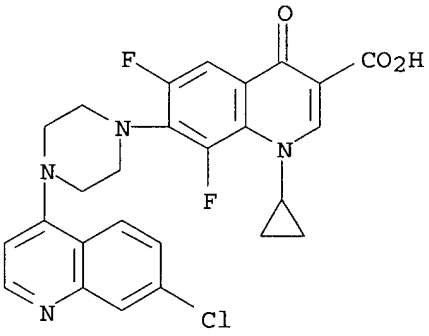
AB Title compds. [I; R1 = C1-C5-alkyl, C1-C5-cycloalkyl; R5 = H, NH2; R8 = H, F; R = 2-pyridyl, 2-pyrimidyl, 2-pyrazinyl, 5-trifluoromethyl-2-pyridyl, 7-chloro-4-benzo[b]pyridinyl, 2-thiazolyl, CO2R3; R3 = CH3, CH3CH2, (CH3)2CHCH2, Cl3CCH2, C1-C5-alkyl, CO; R4 = H, CH3, C1-C5-alkyl; n = 1, 2] are prepared from intermediates (Et 1-cyclopropyl-1,4-dihydro-6,7,8-trifluoro-4-oxoquinoline-3-carboxylate , Et 5-amino-1-cyclopropyl-1,4-dihydro-6,7,8-trifluoro-4-oxoquinoline-3- carboxylate, Et 1,4-dihydro-1-ethyl-6,7,8-trifluoro-4- oxoquinoline-3-carboxylate, Et 7-chloro-1-cyclopropyl-1,4- dihydro-6-fluoro-4-oxoquinoline-3-carboxylate, or Et 7- chloro-1,4-dihydro-1-ethyl-6-fluoro-4-oxoquinoline-3-carboxylate) by condensation with piperazine or homopiperazine derivative in nonpolar organic solvent or substitution with alkyl chloroformate in alkaline solution or organic solvent. Above intermediates are prepared from chlorofluoroaniline, trifluoroaniline, and trifluorobenzoic acid by conventional method. Title compds. are used as anti-mycoplasma agents or for removal of mycoplasma pollution in cell culture. Thus, the title compound II was prepared

IT **291781-44-7P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation of carbostyrils and their use as antimycoplasma agents)

RN 291781-44-7 HCAPLUS
CN 3-Quinolinecarboxylic acid, 7-[4-(7-chloro-4-quinolinyl)-1-piperazinyl]-1-cyclopropyl-6,8-difluoro-1,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



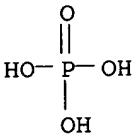
L76 ANSWER 6 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:667339 HCAPLUS
DOCUMENT NUMBER: 133:213090
TITLE: Piperaquine tablet
INVENTOR(S): Li, Guoqiao
PATENT ASSIGNEE(S): Jianqiao Medicine Science & Technology Import & Export Co. Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 4 pp.
CODEN: CNXXEV
DOCUMENT TYPE: **Patent**
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1237416	A	19991208	CN 1998-113233	19980602 <--
CN 1092048	B	20021009		
PRIORITY APPLN. INFO.:			CN 1998-113233	19980602

AB Piperaquine tablet is composed of piperaquine phosphate 25-35, dihydroarteannuin 2-5, trimethoprim 6-12, and primaquine phosphate 1 part. Dihydroarteannuin may be replaced by arteannuin, artesunate, artemether, or arteannuin derivs.
IT **85547-56-4**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antimalarial piperaquine tablet)
RN 85547-56-4 HCAPLUS
CN Quinoline, 4,4'-(1,3-propanediyldi-4,1-piperazinediyl)bis[7-chloro-, phosphate (9CI) (CA INDEX NAME)

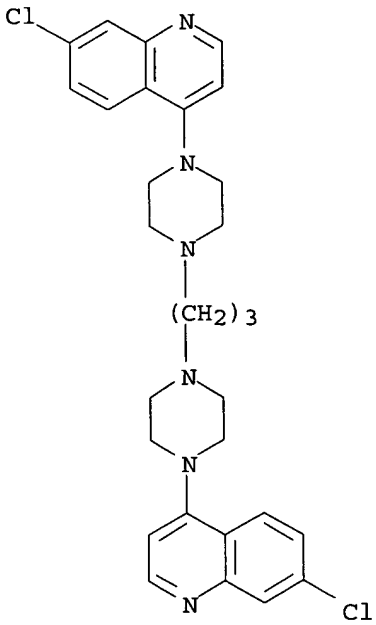
CM 1

CRN 7664-38-2
CMF H3 O4 P



CM 2

CRN 4085-31-8
CMF C29 H32 Cl2 N6



L76 ANSWER 7 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:219795 HCAPLUS
DOCUMENT NUMBER: 128:257447
TITLE: Preparation of nitrogenous heterocyclic compounds inhibiting phosphorylation of platelet-derived growth factors (PDGF) receptors
INVENTOR(S): Matsuno, Kenji; Ichimura, Michio; Nomoto, Yuji; Fujiwara, Shigeki; Ide, Shinichi; Tsukuda, Eiji; Irie, Junko; Oda, Shoji
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: PCT Int. Appl., 312 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9814431	A1	19980409	WO 1997-JP3510	19971001 <--

W: AU, BG, BR, CA, CN, CZ, HU, JP, KR, MX, NO, NZ, PL, RO, SG, SI, SK, UA, US, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

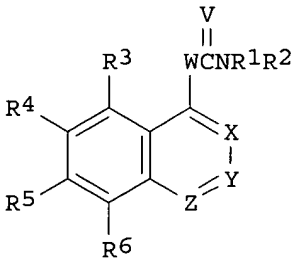
CA 2239227	AA	19980409	CA 1997-2239227	19971001	<--
AU 9744708	A1	19980424	AU 1997-44708	19971001	<--
AU 719392	B2	20000511			
EP 882717	A1	19981209	EP 1997-943133	19971001	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
CN 1208404	A	19990217	CN 1997-191741	19971001	<--
MX 9804356	A	20000831	MX 1998-4356	19980601	<--
US 6169088	B1	20010102	US 1998-88199	19980601	<--
US 6207667	B1	20010327	US 2000-481544	20000112	<--
US 2002068734	A1	20020606	US 2000-734918	20001213	<--
US 6472391	B2	20021029			
US 2003229077	A1	20031211	US 2002-227302	20020826	
US 6750218	B2	20040615			

PRIORITY APPLN. INFO.:

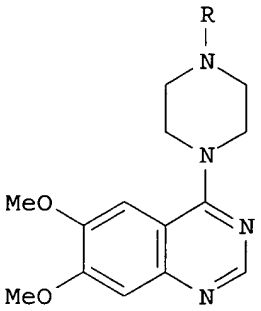
JP 1996-260743	A	19961001
WO 1997-JP3510	W	19971001
US 1998-88199	A3	19980601
US 2000-481544	A3	20000112
US 2000-734918	A3	20001213

OTHER SOURCE(S): MARPAT 128:257447

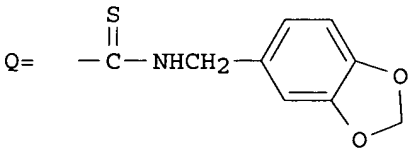
GI



I



II

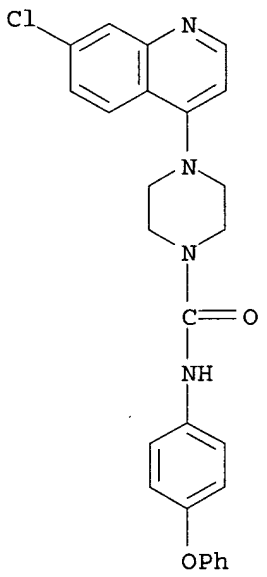


AB Nitrogenous heterocyclic compds. of general formula [I; wherein V is oxygen or sulfur; W is 1,4-piperazinediyl or 1,4-homopiperazinediyl which may be substituted with unsubstituted alkyl on the ring; X is nitrogen or C-R9; Y is nitrogen or C-R8; Z is nitrogen or C-R7, with at least one of X, Y and Z being nitrogen; R1 is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl or the like; R2 is substituted alkyl, substituted or unsubstituted cycloalkyl or the like; R3, R4, R5 and R6 are each independently hydrogen, halogeno, substituted or unsubstituted alkyl, nitro, cyano, (un)substituted OH or NH2 or the like; R7, R8 = R1, halogeno or the like; R9 is hydrogen or acyl] and

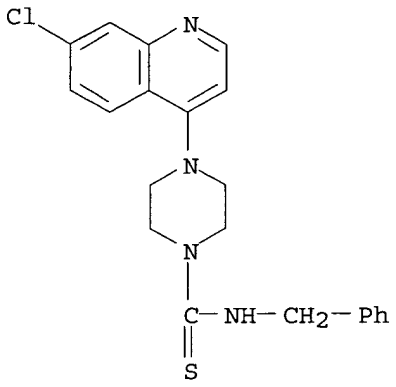
pharmacol. acceptable salts thereof are prepared These compds. inhibit the phosphorylation of PDGF acceptors and the abnormal proliferation or migration of cells and so are effective in preventing or treating cell proliferative diseases such as arterial sclerosis, vascular reocclusion diseases, cancer, and glomerulosclerosis. Thus, 6,7-dimethoxy-4-piperazinylquinazoline was dissolved in ethanol, followed by adding Ph isocyanate, and the resulting mixture was heated at reflux for 10 min to give 4(4-quinazolinyl)piperazine derivative (II; R = CONHPh). II (R = Q) in vitro showed IC50 of 0.03 μM for inhibiting the phosphorylation of PDGF receptor. Pharmaceutical formulations, e.g. tablet containing II (R = N-p-nitrophenylcarbamoyl), were prepared

IT **205255-54-5P 205258-54-4P 205258-55-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of nitrogenous heterocyclic compds. inhibiting phosphorylation of platelet-derived growth factors (PDGF) receptors)

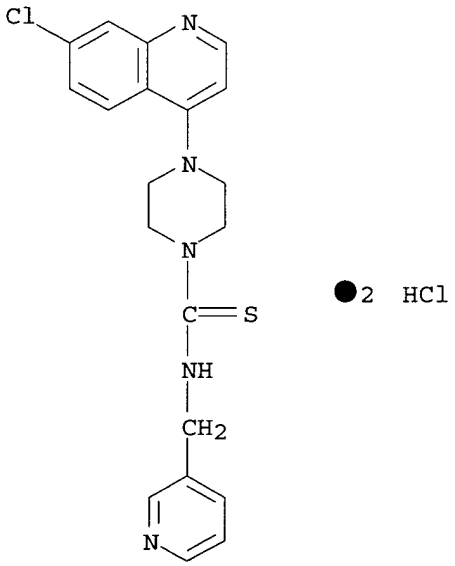
RN 205255-54-5 HCAPLUS
CN 1-Piperazinecarboxamide, 4-(7-chloro-4-quinolinyl)-N-(4-phenoxyphenyl)-(9CI) (CA INDEX NAME)



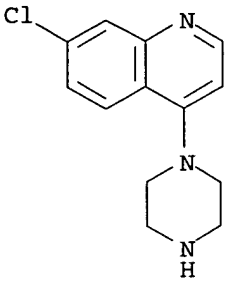
RN 205258-54-4 HCAPLUS
CN 1-Piperazinecarbothioamide, 4-(7-chloro-4-quinolinyl)-N-(phenylmethyl)-(9CI) (CA INDEX NAME)



RN 205258-55-5 HCAPLUS
CN 1-Piperazinecarbothioamide, 4-(7-chloro-4-quinolinyl)-N-(3-pyridinylmethyl)-, dihydrochloride (9CI) (CA INDEX NAME)



IT **837-52-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of nitrogenous heterocyclic compds. inhibiting phosphorylation of platelet-derived growth factors (PDGF) receptors)
RN 837-52-5 HCAPLUS
CN Quinoline, 7-chloro-4-(1-piperazinyl)- (7CI, 8CI, 9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

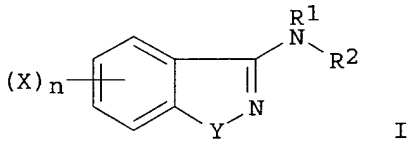
L76 ANSWER 8 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:191579 HCAPLUS
DOCUMENT NUMBER: 124:343282
TITLE: Substituted 3-(aminoalkylamino)-1,2-benzisoxazoles and related compounds useful as antidepressants
INVENTOR(S): O'Malley, Gerard J.; Palermo, Mark G.
PATENT ASSIGNEE(S): Hoechst-Roussel Pharmaceuticals, Inc., USA
SOURCE: U.S., 40 pp., Cont.-in-part of U. S. Ser. No.980,021, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5494908	A	19960227	US 1993-150301	19931112 <--
CA 2149918	AA	19940609	CA 1993-2149918	19931122 <--
WO 9412495	A1	19940609	WO 1993-US11416	19931122 <--
W: AU, CA, FI, JP, KR, NO, NZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 669920	A1	19950906	EP 1994-902374	19931122 <--
EP 669920	B1	20030212		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08506094	T2	19960702	JP 1994-513352	19931122 <--
JP 3462501	B2	20031105		
AT 232529	E	20030215	AT 1994-902374	19931122 <--
ES 2187518	T3	20030616	ES 1994-902374	19931122 <--
PT 669920	T	20030630	PT 1994-902374	19931122 <--
FI 9502481	A	19950522	FI 1995-2481	19950522 <--
NO 9502018	A	19950522	NO 1995-2018	19950522 <--
US 5580982	A	19961203	US 1995-470520	19950606 <--
US 6046203	A	20000404	US 1995-471197	19950606 <--
US 5925766	A	19990720	US 1997-816817	19970318 <--
US 5756754	A	19980526	US 1997-878876	19970619 <--

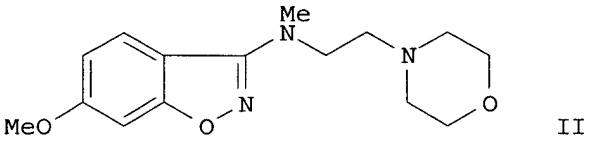
PRIORITY APPLN. INFO.:

US 1992-980021	B2	19921123
US 1993-150301	A	19931112
WO 1993-US11416	W	19931122
US 1995-469278	B1	19950606
US 1995-470393	B1	19950606

OTHER SOURCE(S): MARPAT 124:343282
GI



I



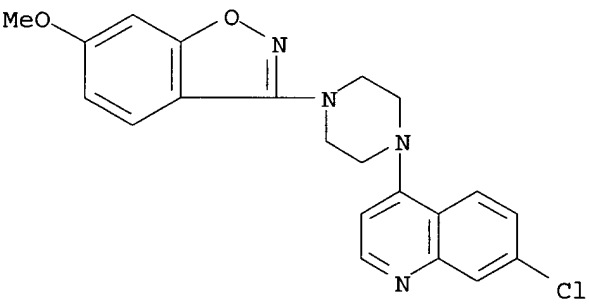
II

AB Title compds. I [R1 = H, alkyl, aralkyl, alkoxycarbonyl, (di)(alkyl)aminocarbonyl, etc.; X = H, alkyl, alkoxy, halo, (un)substituted OH or NH2; Y = O, S, (un)substituted NH; R2 = (CH2)m-Am where Am = (thio)morpholino, (un)substituted NH2, piperidinyl, pyridyl, piperazino; or NR1R2 forms cyclic amine; m = 2-7; n = 0-3] and their pharmaceutically acceptable addition salts, optical and geometric isomers, and racemic mixts. are disclosed. The compds. are useful for treatment of various memory dysfunctions characterized by a decreased cholinergic function such as Alzheimer's disease. The compds. also inhibit monoamine oxidase (MAO), and are useful as antidepressants. For example, 3-chloro-6-methoxy-1,2-benzisoxasole and N-methyl-N-[2-(4-morpholinyl)ethyl]amine were condensed by heating together in a sealed tube at 140° for 48 h to give title compound II. In assays for inhibition of rat mitochondrial MAO (types A and B) in vitro, II had IC50 values of 13 and >103 μM, vs. 0.18 and 23 for the standard brofaromine.

IT **157368-78-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (aminoalkylamino)benzisoxazoles as antidepressants and cholinomimetics)

RN 157368-78-0 HCAPLUS

CN 1,2-Benzisoxazole, 3-[4-(7-chloro-4-quinolinyl)-1-piperazinyl]-6-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



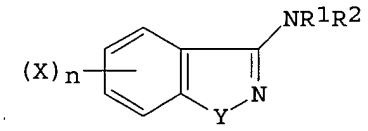
● HCl

L76 ANSWER 9 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN

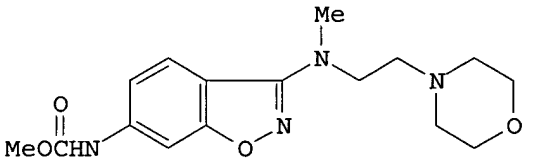
ACCESSION NUMBER: 1994:557676 HCAPLUS
DOCUMENT NUMBER: 121:157676
TITLE: Substituted 3-(aminoalkylamino)-1,2-benzisoxazoles and related compounds
INVENTOR(S): Palermo, Mark G.; O'malley, Gerard J.
PATENT ASSIGNEE(S): Hoechst-Roussel Pharmaceuticals Incorporated, USA
SOURCE: PCT Int. Appl., 114 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
WO 9412495	A1	19940609	WO 1993-US11416		19931122	<--
W: AU, CA, FI, JP, KR, NO, NZ						
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE						
US 5494908	A	19960227	US 1993-150301		19931112	<--
AU 9456765	A1	19940622	AU 1994-56765		19931122	<--
AU 690529	B2	19980430				
EP 669920	A1	19950906	EP 1994-902374		19931122	<--
EP 669920	B1	20030212				
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE						
JP 08506094	T2	19960702	JP 1994-513352		19931122	<--
JP 3462501	B2	20031105				
AT 232529	E	20030215	AT 1994-902374		19931122	<--
FI 9502481	A	19950522	FI 1995-2481		19950522	<--
NO 9502018	A	19950522	NO 1995-2018		19950522	<--
PRIORITY APPLN. INFO.:			US 1992-980021	A	19921123	
			US 1993-150301		19931112	
			WO 1993-US11416	W	19931122	

OTHER SOURCE(S): MARPAT 121:157676
GI



I



II

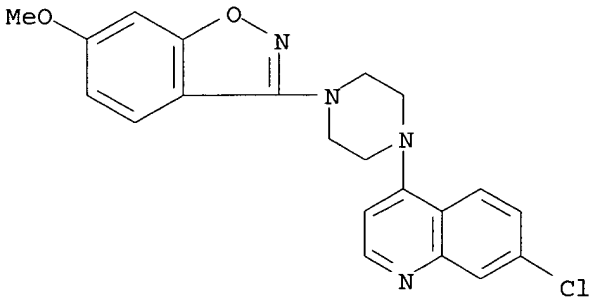
AB The title compds., 3-[(aminoalkyl)amino]-1,2-benzisoxazoles, -benzimidazoles and -1,2-benzothiazoles I (R1 = R1 = H, alkyl, aryl, etc.; R2 = piperazinylalkyl, piperidinylalkyl, morpholinylalkyl, etc.; X = H, alkyl, alkoxy, etc.; Y = oxygen, sulfur, nitrogen) were disclosed. I and pharmaceutically acceptable addition salts thereof and optical and geometric isomers or racemic mixts. thereof are useful for the treatment of various memory dysfunctions characterized by a decreased cholinergic function such

as Alzheimer's disease. Compds. of this invention also inhibit monoamine oxidase and hence are useful as antidepressants. An example compound, Me [3-[methyl[2-(1-morpholinyl)ethyl]amino]-1,2-benzisoxazol-6-yl]carbamate (II) was prepared II inhibited acetylcholinesterase in rat brain in vitro (IC50 = 13 μM).

IT **157368-78-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as cholinesterase inhibitor)

RN 157368-78-0 HCAPLUS

CN 1,2-Benzisoxazole, 3-[4-(7-chloro-4-quinolinyl)-1-piperazinyl]-6-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L76 ANSWER 10 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1989:75336 HCAPLUS

DOCUMENT NUMBER: 110:75336

TITLE: Preparation of 7-chloro-4-hydroxyquinoline N-oxide as anticancer and analgesic agent

INVENTOR(S): Wang, Yubu

PATENT ASSIGNEE(S): Peop. Rep. China

SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 13 pp.
CODEN: CNXXEV

DOCUMENT TYPE: **Patent**

LANGUAGE: Chinese

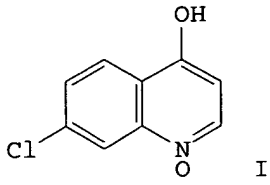
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

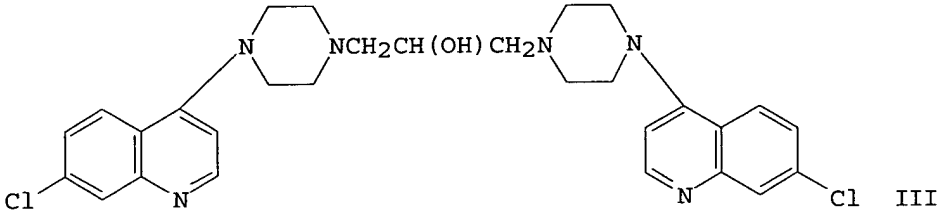
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
CN 86103115	A	19871111	CN 1986-103115	19860429	<--
CN 1009090	B	19900808			

PRIORITY APPLN. INFO.: CN 1986-103115 19860429

GI



I



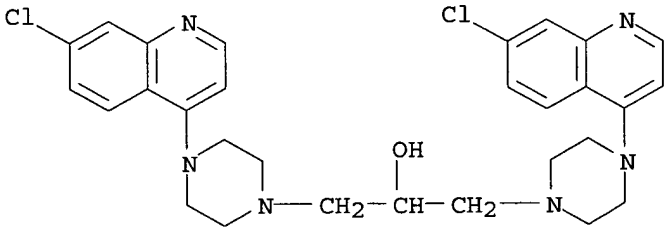
III

AB The title compound (I) is prepared by refluxing 7-chloro-4-hydroxyquinoline (II) or III with H2O2 in organic solvents. I is tested in various forms to show high activity and low toxicity. The oxidation yield is 60-70% with >97% purity. I showed 45.2-48% inhibition of Ehrlich ascites at 100 mg/kg-day in mice and increase in survival rate by 156% at 75 mg/kg-day. I increases pain threshold by 432% at 80 mg/kg i.p. in mice, vs. 293% at 325 mg/kg for dolantin. I showed LD50 at (91 ± 0.04) mg/kg i.p. and (5430 ± 70) mg/kg p.o. I showed no toxic effects on nervous, respiratory, circulatory, or immunity system.

IT **74351-59-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(hydroxylation-oxidation of)

RN 74351-59-0 HCAPLUS

CN 1-Piperazineethanol, 4-(7-chloro-4-quinolinyl)-α-[[4-(7-chloro-4-quinolinyl)-1-piperazinyl]methyl]- (9CI) (CA INDEX NAME)

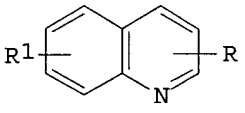


L76 ANSWER 11 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1977:517794 HCAPLUS
DOCUMENT NUMBER: 87:117794
TITLE: Hydroxyalkyl-substituted amino-quinolines
INVENTOR(S): Simpson, William R.
PATENT ASSIGNEE(S): Sandoz, Inc., USA
SOURCE: U.S., 8 pp. Division of U.S. 3,957,791.
CODEN: USXXAM
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4035367	A	19770712	US 1976-656246	19760209 <--
US 3856796	A	19741224	US 1972-291833	19720925 <--
US 3957791	A	19760518	US 1974-504427	19740909 <--
PRIORITY APPLN. INFO.:			US 1971-127376 A2	19710323
			US 1972-245308 A2	19720419
			US 1972-291833 A3	19720925
			US 1974-504427 A3	19740909

GI



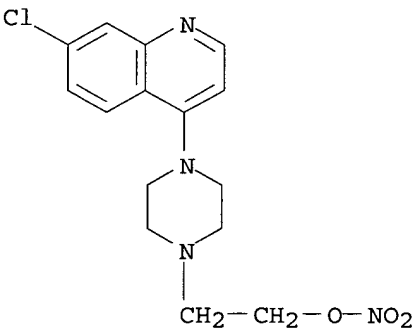
I

AB The aminoquinolines I [R = 2-, 4-(HOCH2CH2)2N(CH2)3NH, 4-(2-hydroxyethyl)piperazino, HOCH2CH(OH)CH2NH, HO(CH2)5NH, HO(CH2)4NH; R1 = H, 6,7-(MeO)2, 7-Cl, 8-MeO, 7-MeO, etc.] were prepared by treating I (R = halo) with RH. I were converted to their nitrate, furmarate, and maleate esters. At 10-150 mg/kg I had antiobesity activity. At 0.2-100 mg/kg I were antihypertensive, antianginal, and antiarrhythmic.

IT **39844-10-5P 39844-41-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 39844-10-5 HCAPLUS

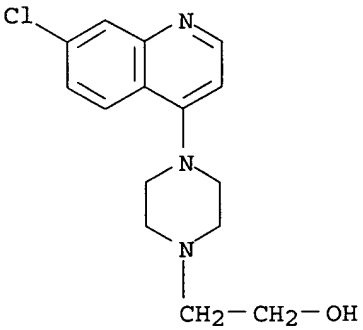
CN 1-Piperazineethanol, 4-(7-chloro-4-quinolinyl)-, nitrate (ester), dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 39844-41-2 HCAPLUS

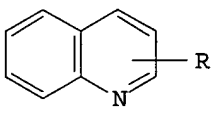
CN 1-Piperazineethanol, 4-(7-chloro-4-quinolinyl)- (9CI) (CA INDEX NAME)



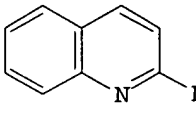
L76 ANSWER 12 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1976:508554 HCAPLUS
DOCUMENT NUMBER: 85:108554
TITLE: Hydroxyalkyl piperazinoquinoline nitrates
INVENTOR(S): Simpson, William R.
PATENT ASSIGNEE(S): Sandoz-Wander, Inc., USA
SOURCE: U.S., 8 pp. Division of U.S. 3,856,796.
CODEN: USXXAM
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
US 3957791	A	19760518	US 1974-504427		19740909	<--
US 3856796	A	19741224	US 1972-291833		19720925	<--
US 4035367	A	19770712	US 1976-656246		19760209	<--
PRIORITY APPLN. INFO.:			US 1971-127376	A2	19710323	
			US 1972-245308	A2	19720419	
			US 1972-291833	A3	19720925	
			US 1974-504427	A3	19740909	

GI



I



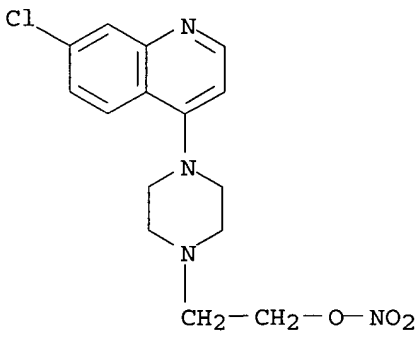
II

AB Hydroxyalkylaminoquinoline nitrates I (R = 2-, 4-hydroxyalkylamino, hydroxyalkylpiperazino, bis(hydroxyalkyl)aminoalkylamino nitrate; aromatic ring may be substituted) (85 compds.) were prepared for use as antihypertensive, antiangina, antiarrhythmic, antiobesity, and peripheral vasodilator agents (no data). Thus, 2-chloroquinoline was treated with (HOCH2CH2)2N(CH2)3NH2 and the product treated with HNO3 in AcO2-HOAc to give II.

IT **39844-10-5P 39844-41-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

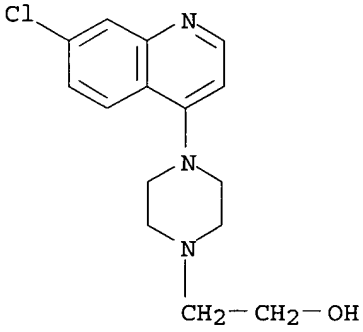
RN 39844-10-5 HCAPLUS
CN 1-Piperazineethanol, 4-(7-chloro-4-quinolinyl)-, nitrate (ester),

dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 39844-41-2 HCAPLUS
CN 1-Piperazineethanol, 4-(7-chloro-4-quinolinyl)- (9CI) (CA INDEX NAME)



L76 ANSWER 13 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1973:4143 HCAPLUS
DOCUMENT NUMBER: 78:4143
TITLE: Pharmacologically active quinoline derivatives
INVENTOR(S): Simpson, William R. J.
PATENT ASSIGNEE(S): Sandoz Ltd.
SOURCE: Ger. Offen., 35 pp.
CODEN: GWXXBX
DOCUMENT TYPE: **Patent**
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
DE 2214051	A	19721005	DE 1972-2214051	19720323	<--
NL 7203479	A	19720926	NL 1972-3479	19720316	<--
BE 781013	A1	19720921	BE 1972-115371	19720321	<--
DD 100253	C	19730912	DD 1972-161691	19720321	<--
HU 165249	P	19740727	HU 1972-SA2331	19720321	<--

GB 1374339	A	19741120	GB 1972-13102		19720321 <--
ES 401024	A1	19750901	ES 1972-401024		19720321 <--
FR 2130520	A5	19721103	FR 1972-9933		19720322 <--
FR 2130520	B1	19751226			
AT 7202432	A	19750615	AT 1972-2432		19720322 <--

PRIORITY APPLN. INFO.: US 1971-127376 A 19710323

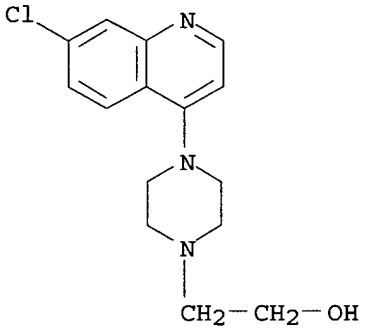
GI For diagram(s), see printed CA Issue.

AB Hydroxyalkylaminoquinoline nitrates I (R = NH(CH2)3N(CH2CH2ONO2)2, NMe(CH2)3N(CH2CH2ONO2)2, NH(CH2)5ONO2, NHCH2CH(ONO2)CH2ONO2, 4-(2-hydroxyethyl)piperazino nitrate in the 2-, 3-, or 4-position; R1. R3 = H, MeO; R2 = Cl, H, MeO) and their methiodides were prepared by treating the corresponding chloroquinoline with a hydroxyalkyl amine and nitrating in the presence of HOAc.

IT **39844-41-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(nitration of)

RN 39844-41-2 HCAPLUS

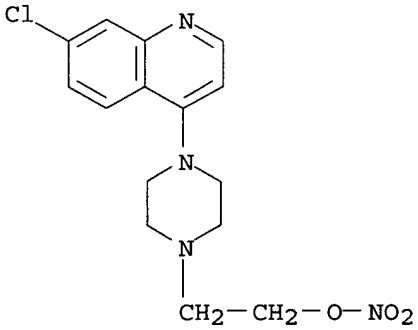
CN 1-Piperazineethanol, 4-(7-chloro-4-quinolinyl)- (9CI) (CA INDEX NAME)



IT **39844-10-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 39844-10-5 HCAPLUS

CN 1-Piperazineethanol, 4-(7-chloro-4-quinolinyl)-, nitrate (ester), dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L76 ANSWER 14 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1967:490839 HCAPLUS
DOCUMENT NUMBER: 67:90839
TITLE: 1-Substituted-4-substituted aminoalkylenepiperazines
INVENTOR(S): Tomcufcik, Andrew S.; Fabio, Paul F.; Hoffman, Arlene M.
PATENT ASSIGNEE(S): American Cyanamid Co.
SOURCE: U.S., 7 pp.
CODEN: USXXAM
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

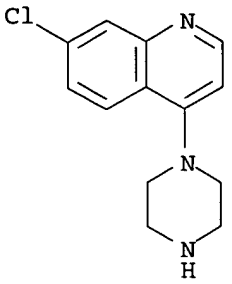
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3331843		19670718	US	19630404 <--
FR 1528557			FR	

GI For diagram(s), see printed CA Issue.

AB 1-Substituted-4-substituted aminopropylenepiperazines, I, where R is a heterocyclic group are prepared by treating a 1-(3-disubstituted aminopropylene)piperazine with a haloheterocyclic compound, a haloheterocyclic substituted piperazine with a ω-disubstituted aminopropylene halide, or by several differing reactions. Thus, to a mixture of 8.6 g. 1-(3-dimethylaminopropyl)piperazine and 4.2 g. NaHCO3 in 200 ml. Cellosolve was added 10.5 4,7-dichloroquinoline. The mixture was refluxed 16.5 hrs., cooled, filtered, and the filtrate stripped of solvent. The residue in 100 ml. MeOH was treated with 37.5 ml. 8N methanolic HCl, ether added to precipitate the product, the mixture filtered, and the crude product treated with activated C to give 7.3 g. 1-(7-chloro-4-quinolyl)-4-(3-dimethylaminopropyl)piperazine-3HCl.H2O, m. 263° (MeOH) (decomposition). Also claimed were [R, salt, and salt m.p. given]: 7-chloro-4-quinolyl, 3HCl, 277° (isopropanol-MeOH) (decomposition); 7-chloro-4-quinolyl, trimaleate, 159-61° (decomposition); 5-nitro-2-pyridyl, 2HCl, 260° (decomposition); 5-nitro-2-thiazolyl, 2HCl, 260-70° (decomposition); 2-pyridyl, 3HCl, 258-65° (decomposition); 2-quinolyl, -, -; 2-benzoxazoyl, 2 HCl, 275-95° (decomposition); 2-benzothiazolyl, -, 92-4°; 4-pyridyl, trimaleate, 177-9°; 6-methoxy-8-quinolyl, trimaleate, 177-80° (EtOH); 2-thiazolyl dimaleate, 164-5°; 1,3,4-thiadiazol-2-yl, dimaleate, 164-6°; 4-quinolyl 1-oxide, trimaleate, 118-20°; 5-benzamido-2-pyridyl, dimaleate, 164-5°. Also claimed are 1-(2-benzothiazolyl)-trans-2,5-dimethyl-4-(3-dimethylaminopropyl)piperazine, and 1-(7-chloro-4-quinolyl)piperazine.

IT **837-52-5P 900-57-2P 901-97-3P**
954-51-8P 954-52-9P 1063-52-1P
1252-78-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

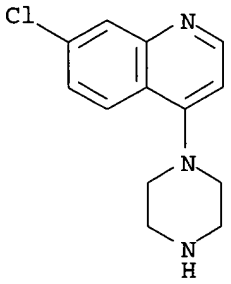
RN 837-52-5 HCAPLUS
CN Quinoline, 7-chloro-4-(1-piperazinyl)- (7CI, 8CI, 9CI) (CA INDEX NAME)



RN 900-57-2 HCAPLUS
CN Quinoline, 7-chloro-4-(1-piperazinyl)-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

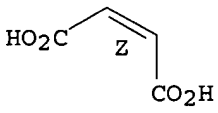
CRN 837-52-5
CMF C13 H14 Cl N3



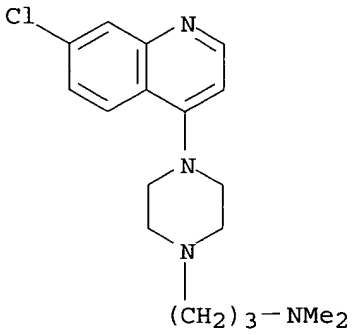
CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.

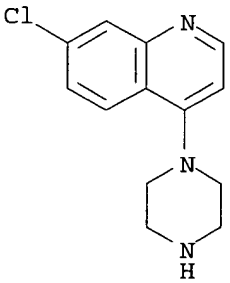


RN 901-97-3 HCAPLUS
CN Quinoline, 7-chloro-4-[4-[3-(dimethylamino)propyl]-1-piperazinyl]-, trihydrochloride (7CI, 8CI) (CA INDEX NAME)



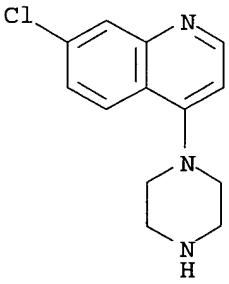
●3 HCl

RN 954-51-8 HCAPLUS
CN Quinoline, 7-chloro-4-(1-piperazinyl)-, dihydrobromide (8CI) (CA INDEX NAME)



●2 HBr

RN 954-52-9 HCAPLUS
CN Quinoline, 7-chloro-4-(1-piperazinyl)-, dihydrochloride (8CI) (CA INDEX NAME)

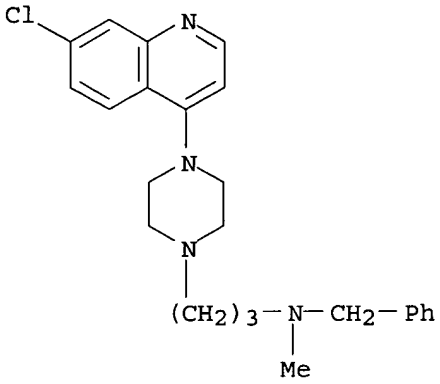


●2 HCl

RN 1063-52-1 HCAPLUS
CN Quinoline, 4-[4-[3-(benzylmethylamino)propyl]-1-piperazinyl]-7-chloro-, maleate (1:3) (8CI) (CA INDEX NAME)

CM 1

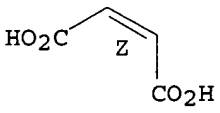
CRN 1057-17-6
CMF C24 H29 Cl N4



CM 2

CRN 110-16-7
CMF C4 H4 O4

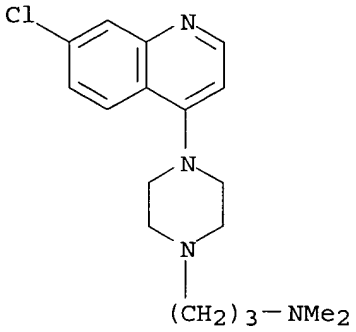
Double bond geometry as shown.



RN 1252-78-4 HCAPLUS
CN Quinoline, 7-chloro-4-[4-[3-(dimethylamino)propyl]-1-piperazinyl]-, maleate (1:3) (8CI) (CA INDEX NAME)

CM 1

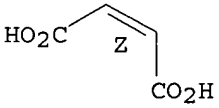
CRN 298-78-2
CMF C18 H25 Cl N4



CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



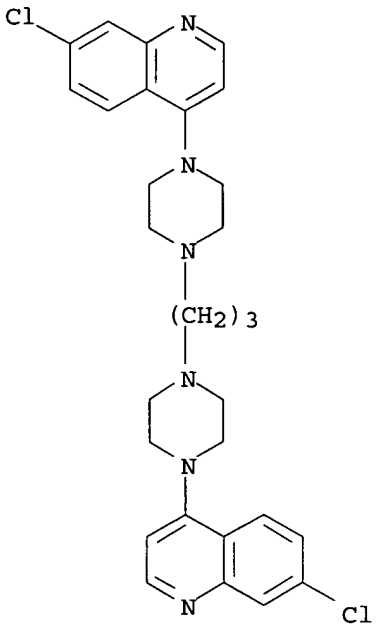
L76 ANSWER 15 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1965:480716 HCAPLUS
DOCUMENT NUMBER: 63:80716
ORIGINAL REFERENCE NO.: 63:14883h,14884a
TITLE: 1,3-Bis[4-(4-quinolyl)-1-piperazino]propane
PATENT ASSIGNEE(S): Rhone-Poulenc SA
SOURCE: 8 pp.
DOCUMENT TYPE: **Patent**
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR M3266		19650531	FR	19630530 <--

AB 1,3-Bis[4-(7-chloro-4-quinolyl)-1-piperazino]propane (I) is prepared and is useful as an anthelmintic or antimalarial agent or as an amebicide. Thus, a mixture of 1-[4-(7-chloro-4-quinolyl)-1-piperazino]-3-(1-piperazino)propane 7.5, 4,7-dichloroquinoline 4, and PhOH 11.5 g. is heated 6 hrs. at 135° and added to a solution of 15 g. NaOH in 150 ml. H2O. The mixture is extracted with 350 ml. CHCl3, and the CHCl3 solution washed with a solution of 13 g. MeSO3H in 175 ml. H2O. The acidic solution is made alkaline with 10 g. NaOH in 50 ml. H2O. The solution is extracted with 250 ml. CHCl3, the extract chromatographed on 100 g. Al2O3, the column eluted with 300 ml. CH2Cl2, and the eluate heated to dryness to give 1.8 g. I, m. 199-200° (MeCN), which can be administered at 0.5-15 mg. I/kg. animal. Tablets or pills, each weighing 500 mg., are prepared from 250 mg. I, 190 mg. starch, 50 mg. levilite [sic], and 10 mg. Mg stearate.

IT **4085-31-8**, Quinoline, 4,4'-(trimethylenedi-4,1-

piperazinediyl)bis[7-chloro-
(preparation of)
RN 4085-31-8 HCAPLUS
CN Quinoline, 4,4'-(1,3-propanediyldi-4,1-piperazinediyl)bis[7-chloro- (9CI) (CA INDEX NAME)



L76 ANSWER 16 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1965:472086 HCAPLUS
DOCUMENT NUMBER: 63:72086
ORIGINAL REFERENCE NO.: 63:13290h,13291a-g
TITLE: Quinoline derivatives
PATENT ASSIGNEE(S): Rhone-Poulenc SA
SOURCE: 17 pp.
DOCUMENT TYPE: **Patent**
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

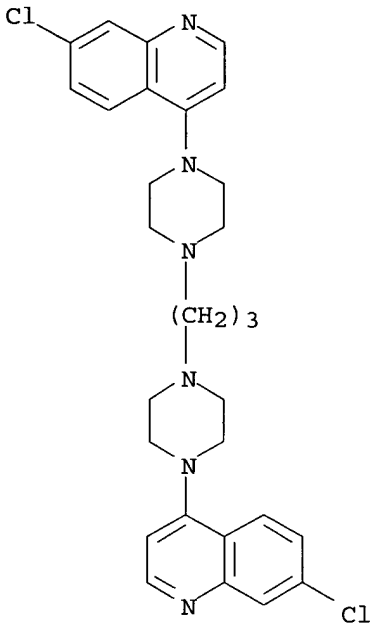
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 84902		19650507	FR	19620830 <--

GI For diagram(s), see printed CA Issue.
AB The preparation of compds. of the general formula (I) is described. A mixture of
50 g. 1,4-bis(piperazin-1-yl)butane (II), 87.5 g. 4,7-dichloroquinoline (IIa), and 94 g. PhOH was heated to 140° whereupon spontaneous reaction occurred with a temperature rise to 170°. The mixture was kept 1 hr. at 150°, cooled to 100°, poured into 1100 ml. distilled H2O containing 64 g. NaOH, and extracted with 2.5 l. CH2Cl2. The organic layer was shaken with 56.5 g. MeSO3H in 1 l. H2O, treated with 3 g. charcoal, and filtered, and the filtrate basified with 85 ml. NaOH solution (d. 1.33) to give 90 g. oil which afforded 57 g. I [X = Cl, R = (CH2)4] (III), m. 178-80° [(iso-Pr)2O]. Chromatography on an Al2O3 column gave pure III, m. 185-6°. Condensation of 152 g. N-benzylpiperazine with

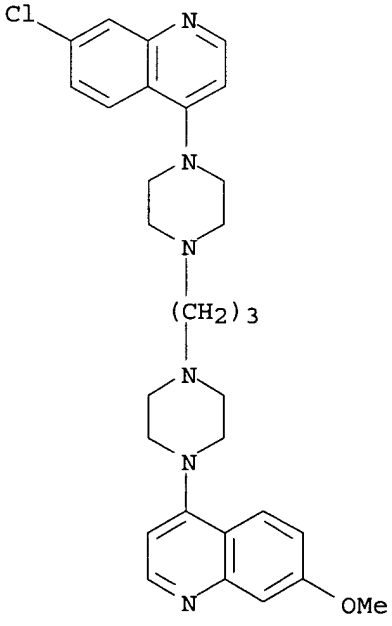
66.5 g. succinoyl chloride in Me2CO in the presence of Et3N yielded 1,4-bis(4-benzyl-1-piperazinyl)-1,4-dioxobutane (IV), m. 156-7°. Reduction of 127 g. IV with LiAlH4 gave 120 g. 1,4-bis(4-benzyl-1-piperazinyl)butane which was debenzylated to give II. To a mixture of 49.5 g. N-(7-chloro-4-quinolyl)piperazine (V), 20.2 g. Et3N, and 200 ml. CHCl3 was added 21.4 g. trans-1,4-dibromo-2-butene in 50 ml. CHCl3 over 20 min. at 25°. Refluxing 1 hr., evaporating in vacuo, and pouring into H2O gave 29 g. I (X = Cl, R = trans-CH2CH:CHCH2) (V), m. 192-4° (BuOH), solidifying and remelting at 200°. Hydrogenation of 2.75 g. V and 1.92 g. MeSO3H in 100 ml. MeOH over 0.5 g. PrO2 and basification of the product with NaOH gave 1.2 g. II. Similarly, from 124 g. V, 300 ml. C6H6, and ClCH2C.tplbond.CCH2Cl (VI) was obtained 63 g. I (X = Cl, R = CH2C.tplbond.CCH2) (VII), which was purified by treatment with MeSO3H to give 25 g. VII, m. 202-3°. VI, b0.1 32-4°, was prepared by chlorination of 16 g. HOCH2C.tplbond.CCH2OH in C5H5N. Hydrogenation of VII in the presence of PtO2 gave III. A mixture of 28.2 g. I [X = Cl, R = CO(CH2)3] (VIII), 7.6 g. LiAlH4 and 515 ml. tetrahydrofuran was refluxed 4 hrs., the mixture treated with 7.6 ml. H2O and then with 1.1 g. NaOH in 7.5 ml. H2O, and the solid collected and crystallized from 225 ml. MeCOEt and chromatographed on Al2O3 to give 0.22 g. III. VIII (76.6 g.), m. 140-3°, was obtained from the reaction of 74.3 g. V and 105 g. IX (picrate, m. 227-9°). Treatment of 74.3 g. V with 42.3 g. ClCO(CH2)3Cl gave 105 g. IX. Heating a mixture of 7.5 g. X, 4 g. IIa, and 11.5 g. PhOH 6 hrs. at 135° and working up as in the 1st example and chromatographing the impure product on Al2O3 gave 1.8 g. I [X = Cl, R = (CH2)3] (XI), m. 199-200°. Reaction of 68 g. IX with 38.9 g. ethoxycarbonylpiperazine gave the N-ethoxycarbonyl derivative of X, 89 g. of which on hydrolysis and decarboxylation gave 74.7 g. X. XI was obtained as a monohydrate, m. 70-80°, by crystallization from aqueous EtOH the product obtained by heating 39.6 g. IIa, 21.2 g. 1,3-bis(piperazino)propane, and 37.7 g. PhOH 20 hrs. at 130°. A mixture of 13.5 g. 1-[1-(7-chloro-4-quinolyl)-4-piperazinyl]-3-chloropropane (XII), 10.3 g. 1-(6-chloro-4-quinolyl)piperazine (XIII), 6.2 g. NaI, 4.16 g. Et3N, and 125 ml. MeCOEt was refluxed 6 hrs., cooled, and basified with 500 ml. N NaOH to give 11.3 g. XIV (X = Y = Cl, Z = H), m. 95°. Condensation of 173 g. 1-(3-hydroxypropyl)piperazine with 198 g. IIa gave 160 g. 3-[1-(7-chloro-4-quinolyl)-4-piperazinyl]propanol (XV). Refluxing XV with SOCl2in CHCl3 gave 70.7 g. XII, m. 84°. Similarly, 10.4 g. XIII and 13.5 g. 1-[1-(7-methoxy-4-quinolyl)-4-piperazinyl]3-chloropropane (XVI) gave 10.2 g. XIV (X = MeO, Y = Cl, Z = H), m. 136-8°. XIV (X = MeO, Y = H, Z = Cl), m. 176°, was likewise prepared XVI, m. 103°, was prepared similarly to XII from 3-[1-(7-methoxy-4-quinolyl)-4-piperazinyl] propanol. 1(7-Methoxy-4-quinolyl)piperazine (12.5 g.), m. 146°, was obtained from 19.3 g. 7-methoxy-4-chloroquinoline and 39.8 g. piperazine hydrate in 410 ml. N HCl.

IT **4038-99-7**, Quinoline, 7-chloro-4-[4-(3-chloropropyl)-1-piperazinyl]- **4039-00-3**, Quinoline, 7-chloro-4-[4-[3-(1-piperazinyl)propyl]-1-piperazinyl]- **4039-02-5**, Quinoline, 4,4'-(2-butynylenedi-4,1-piperazinediyl)bis[7-chloro- **4085-31-8**, Quinoline, 4,4'-(trimethylenedi-4,1-piperazinediyl)bis[7-chloro- **4086-55-9**, Quinoline, 7-chloro-7'-methoxy-4,4'-(trimethylenedi-4,1-piperazinediyl)di- **4086-56-0**, Piperazine, 1-(4-chlorobutyryl)-4-(7-chloro-4-quinolyl)- **4180-36-3**, 1-Piperazinecarboxylic acid, 4-[3-[4-(7-chloro-4-quinolyl)-1-piperazinyl]propyl]-, ethyl ester **4257-08-3**, Piperazine, 1-(4-chlorobutyryl)-4-(7-chloro-4-quinolyl)-, picrate **4257-09-4**, Quinoline, 4,4'-(tetramethylenedi-4,1-piperazinediyl)bis[7-chloro- **4407-18-5**, Quinoline, 6,7'-dichloro-4,4'-(trimethylenedi-4,1-piperazinediyl)di- **4914-50-5**, Piperazine, 1-(7-chloro-4-quinolyl)-4-[4-[4-(7-chloro-4-quinolyl)-1-piperazinyl]butyryl]-

RN 4085-31-8 HCAPLUS
CN Quinoline, 4,4'-(1,3-propanediyldi-4,1-piperazinediyl)bis[7-chloro- (9CI) (CA INDEX NAME)

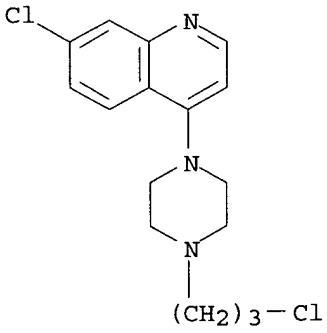


RN 4086-55-9 HCAPLUS
CN Quinoline, 7-chloro-7'-methoxy-4,4'-(trimethylenedi-4,1-piperazinediyl)di- (8CI) (CA INDEX NAME)

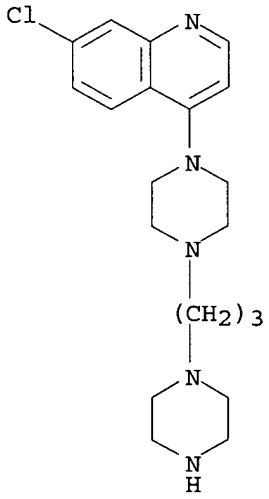


RN 4086-56-0 HCAPLUS
CN Piperazine, 1-(4-chlorobutyryl)-4-(7-chloro-4-quinolyl)- (7CI, 8CI) (CA

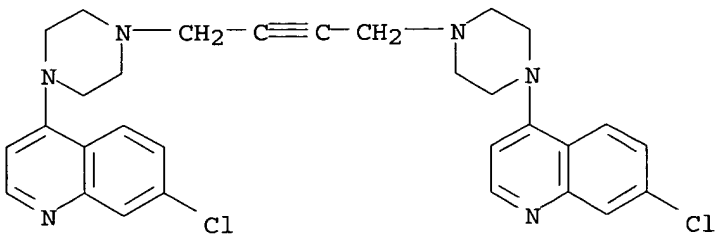
(preparation of)
RN 4038-99-7 HCAPLUS
CN Quinoline, 7-chloro-4-[4-(3-chloropropyl)-1-piperazinyl]- (7CI, 8CI) (CA INDEX NAME)

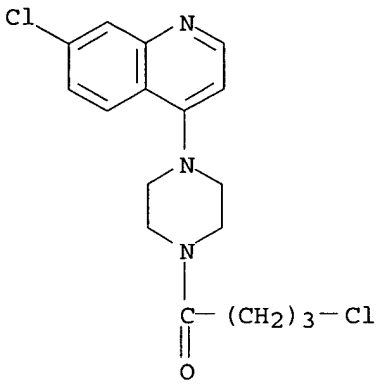


RN 4039-00-3 HCAPLUS
CN Quinoline, 7-chloro-4-[4-[3-(1-piperazinyl)propyl]-1-piperazinyl]- (7CI, 8CI) (CA INDEX NAME)



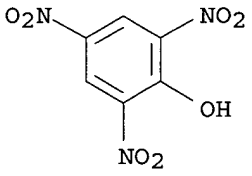
RN 4039-02-5 HCAPLUS
CN Quinoline, 4,4'-(2-butynylenedi-4,1-piperazinediyl)bis[7-chloro- (7CI, 8CI) (CA INDEX NAME)



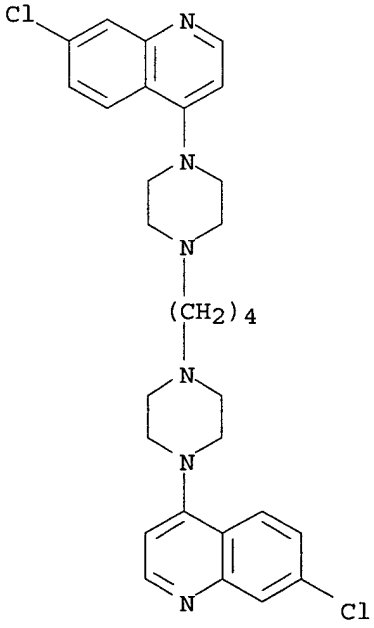


CM 2

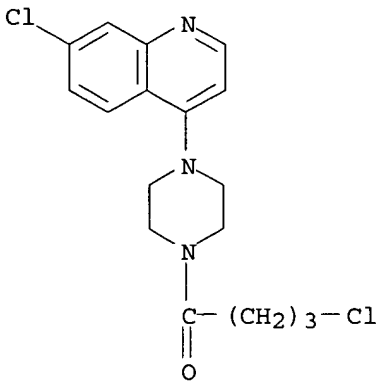
CRN 88-89-1
CMF C6 H3 N3 O7



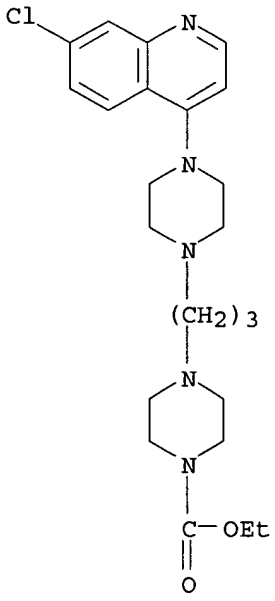
RN 4257-09-4 HCAPLUS
CN Quinoline, 4,4'-(tetramethylenedi-4,1-piperazinediyl)bis[7-chloro- (7CI, 8CI) (CA INDEX NAME)



INDEX NAME)



RN 4180-36-3 HCAPLUS
CN 1-Piperazinecarboxylic acid, 4-[3-[4-(7-chloro-4-quinolyl)-1-piperazinyl]propyl]-, ethyl ester (7CI, 8CI) (CA INDEX NAME)

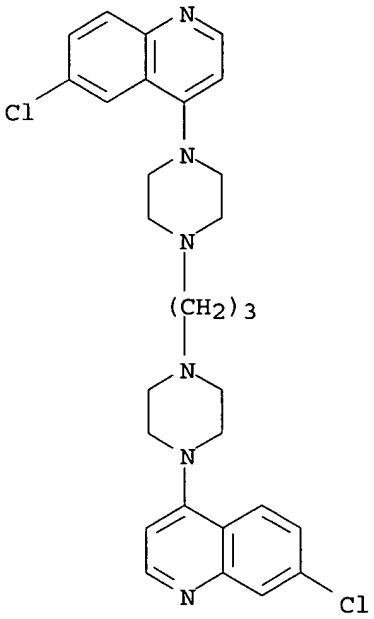


RN 4257-08-3 HCAPLUS
CN Piperazine, 1-(4-chlorobutyryl)-4-(7-chloro-4-quinolyl)-, picrate (8CI) (CA INDEX NAME)

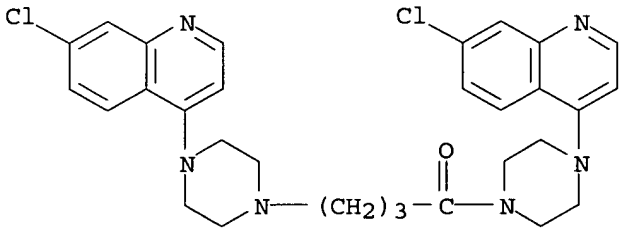
CM 1

CRN 4086-56-0
CMF C17 H19 Cl2 N3 O

RN 4407-18-5 HCAPLUS
CN Quinoline, 6,7'-dichloro-4,4'-(trimethylenedi-4,1-piperazinediyl)di- (7CI, 8CI) (CA INDEX NAME)



RN 4914-50-5 HCAPLUS
CN Piperazine, 1-(7-chloro-4-quinolyl)-4-[4-[4-(7-chloro-4-quinolyl)-1-piperazinyl]butyryl]- (7CI, 8CI) (CA INDEX NAME)



L76 ANSWER 17 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1965:66595 HCAPLUS
DOCUMENT NUMBER: 62:66595
ORIGINAL REFERENCE NO.: 62:11830e-h,11831a-b
TITLE: 1,4-Disubstituted piperazines
INVENTOR(S): Tomcufcik, Andrew S.; Fabio, Paul F.; Hoffman, Arlene M.
PATENT ASSIGNEE(S): American Cyanamid Co.
SOURCE: 62 pp.
DOCUMENT TYPE: **Patent**
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

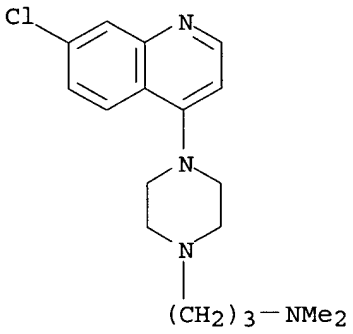
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
BE 637271		19640311	BE	<--
GB 1047935			GB	
NL 297170			NL	
PRIORITY APPLN. INFO.:			US	19630404

AB The title compds. prepared were effective against Trypanosoma. Thus, to 8.6 g. N-(3-dimethylaminopropyl)piperazine (I) and 4.2 g. NaHCO3 in 200 cc. MeOCH2CH2OH was added 10.5 g. 4,7-dichloroquinoline (II), the mixture refluxed 16.5 hrs., the whole filtered, the filtrate evaporated in vacuo, the oil dissolved in 100 cc. MeOH, this solution treated with 37.5 cc. 8N MeOH-HCl, and Et2O added to give 32.3% III [R = Me2N(CH2)3, R1 = 7-chloro-4-quinolyl] (IV), tri-HCl salt hydrate, m. 263° (decomposition) (MeOH); also obtained from I, II, and PhOH in 48.9% yield, isolated as the tri-HCl salt, m. 277° (decomposition) (iso-PrOH-MeOH); IV trimaleate m. 159-61° (decomposition). The following III [R = Me2N(CH2)3] were prepared [R1, m.p., salt, and its m.p. given (m.p. marked with * indicates decomposition point)]: 5-nitro-2-pyridyl, --, di-HCl, *260°; 5-nitro 2-thiazolyl, -- di-HCl, *260-70°; 6-purinyl, 218-20°, --; --; 2-pyridyl, --, tri-HCl, *258-65°; 2-benzothiazolyl, 92-4°, dimethosulfate, *169-73°; 5-nitro-1,3,4-thiadiazol-2-yl, --, dimaleate, *159-62°; 5-bromo-2-pyrimidinyl, --, di-HCl, *290°; 2-quinolyl,--, tri-HCl, *274-80°; 2-benzoxazolyl, --, di-HCl, *265-95°; 4-pyridyl, --, trimaleate, 177-9°; 6-methoxy-4-quinolyl, --, trimaleate, 177-80° (EtOH); 2-pyrazinyl, --, dimaleate, 182-4°; 4-quinazolinyl, --, trimaleate, *152°; 2-thiazolyl, --, dimaleate, 164-5°; 6-phenylimidazo[2,1-b]1,3,4-thiadiazol-2-yl, --, dimaleate, *175-8°; 6-ethoxy-2-benzothiazolyl, 90-2°,-- ,--; 9-acridinyl, 100-2°, --, --; 4,6-diamino-1,3,5-triazin-2-yl, 99°, --, --; 6-phenanthridinyl, --, trimaleate, 155-7°; 1,3,4-thiadiazol-2-yl, --, dimaleate, 157-60°; 4-quinolyl N-oxide, --, trimaleate, 118-20°; 4-quinolyl, --, trimaleate, 158-9°; 6-chloro-2-pyrazinyl, --, dimaleate, 168-70°; Ph, 180-2°, tri-HCl, *235-40°; 3-ClC6H4, --, dimaleate, *172-3°; 4-NO2C6H4, --, di-HCl, *263° (EtOH); 4-AcNHC6H4, --, dimaleate, *147-9° (MeOH); 2,4,6-(NO2)3C6H2, --HCl, *218-20° (MeOH); 4-MeOC6H4, -- dimaleate, 162-3°; Bz, --, di-HCl, *274-8° (MeOH); iso-BuCO2, --, di-HCl, *266°; 3,4,5-(MeO)3C6H2CO, --, di-HCl, *263-5°; PhCH2CO2, --, di-HCl, *218-19° (EtOH); 2,4-Cl2C6H3CO,--, di-HCl, *265-70° (MeOH); 2-furoyl, --, di-HCl, *268°; 2-phenyl-2H-1,2,3-triazol-4-oyl, --, dimaleate, 176-7°; octyloxycarbonyl,--, di-HCl, *258-9°; Cl3CCO, --, di-HCl, *240-5°; 9,10-anthraquinon-2-carbonyl, --, di-HCl, *296°. The trimaleate of III [R = Me(PhCH2)N(CH2)3, R1 = 7-chloro-4-quinolyl] m. 133-5° (decomposition). II, piperazine, and PhOH gave 69% yellow III (R = H, R1 = 7-chloro-4-quinolyl), m. 113.5-14.5° (cyclohexane); di-HBr salt m. 266° (decomposition); di-HCl-0.5H2O salt m. 280° (decomposition); acid maleate m. 167° (decomposition). Piperazine (500 g.), 460 g. Me2N(CH2)3Cl.HCl, and 550 g. NaHCO3 in 2.5 l. EtOH refluxed 7 hrs. gave 207 g. I, b6 96-101°, n26D 1.4750. The following trans-2,5-dimethylpiperazines were prepared (substituent at 1, 4, salt, and its m.p. given): H, Me2N(CH2)3, HCl, 230-5° (decomposition); Me2N(CH2)4, 4-O2NC6H4, di-HCl, 225-33° (decomposition); Bz, Me2N(CH2)3, dimaleate, 243-4° (decomposition); Bz, Me2N(CH2)4, di-HCl, 233-40° (decomposition). The trimaleate of III [R = Me2N(CH2)4, R1 = 7-chloro-4-quinolyl] m. 118-20°; III [R = Bz, R1 = Me2N(CH2)4] di-HCl salt m. 270-1° (decomposition).

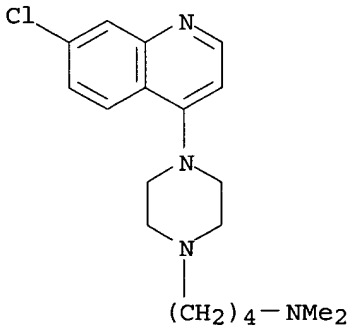
IT **298-78-2**, Quinoline, 7-chloro-4-[4-[3-(dimethylamino)propyl]-1-piperazinyl]- **743-73-7**, Quinoline, 7-chloro-4-[4-[4-

(dimethylamino)butyl]-1-piperazinyl]- **803-78-1**, Quinoline, 7-chloro-4-[4-[4-(dimethylamino)butyl]-2,5-dimethyl-1-piperazinyl]- **837-52-5**, Quinoline, 7-chloro-4-(1-piperazinyl)- **900-57-2**, Quinoline, 7-chloro-4-(1-piperazinyl)-, maleate (1:1) **901-97-3**, Quinoline, 7-chloro-4-[4-[3-(dimethylamino)propyl]-1-piperazinyl]-, trihydrochloride **954-51-8**, Quinoline, 7-chloro-4-(1-piperazinyl)-, dihydrobromide **954-52-9**, Quinoline, 7-chloro-4-(1-piperazinyl)-, dihydrochloride **1057-17-6**, Quinoline, 4-[4-[3-(benzylmethylamino)propyl]-1-piperazinyl]-7-chloro- **1063-52-1**, Quinoline, 4-[4-[3-(benzylmethylamino)propyl]-1-piperazinyl]-7-chloro-, maleate (1:3) **1105-86-8**, Quinoline, 7-chloro-4-[4-[4-(dimethylamino)butyl]-1-piperazinyl]-, maleate (1:3) **1252-78-4**, Quinoline, 7-chloro-4-[4-[3-(dimethylamino)propyl]-1-piperazinyl]-, maleate (1:3)
(preparation of)

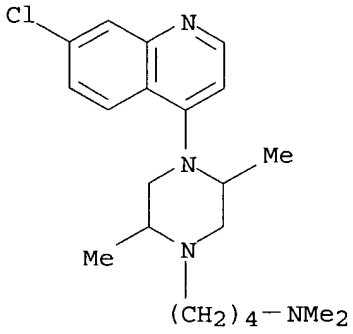
RN 298-78-2 HCAPLUS
CN 1-Piperazinepropanamine, 4-(7-chloro-4-quinolinyl)-N,N-dimethyl- (9CI) (CA INDEX NAME)



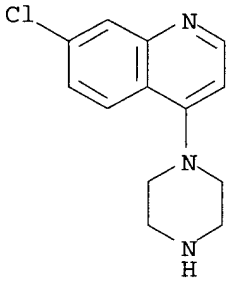
RN 743-73-7 HCAPLUS
CN Quinoline, 7-chloro-4-[4-[4-(dimethylamino)butyl]-1-piperazinyl]- (7CI, 8CI) (CA INDEX NAME)



RN 803-78-1 HCAPLUS
CN Quinoline, 7-chloro-4-[4-[4-(dimethylamino)butyl]-2,5-dimethyl-1-piperazinyl]- (7CI, 8CI) (CA INDEX NAME)



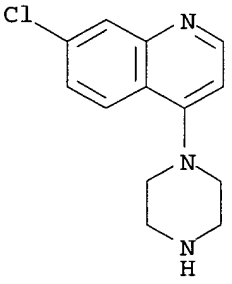
RN 837-52-5 HCAPLUS
CN Quinoline, 7-chloro-4-(1-piperazinyl)- (7CI, 8CI, 9CI) (CA INDEX NAME)



RN 900-57-2 HCAPLUS
CN Quinoline, 7-chloro-4-(1-piperazinyl)-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

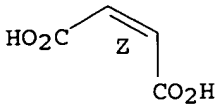
CRN 837-52-5
CMF C13 H14 Cl N3



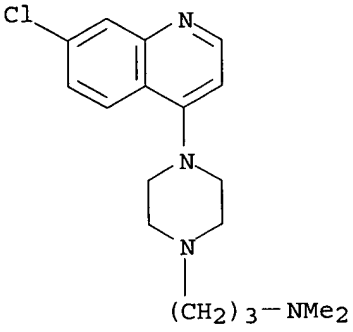
CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.

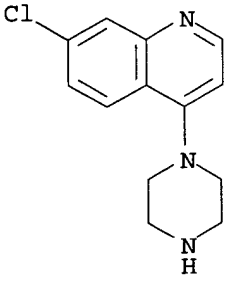


RN 901-97-3 HCAPLUS
CN Quinoline, 7-chloro-4-[4-[3-(dimethylamino)propyl]-1-piperazinyl]-, trihydrochloride (7CI, 8CI) (CA INDEX NAME)



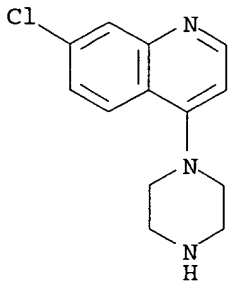
●3 HCl

RN 954-51-8 HCAPLUS
CN Quinoline, 7-chloro-4-(1-piperazinyl)-, dihydrobromide (8CI) (CA INDEX NAME)



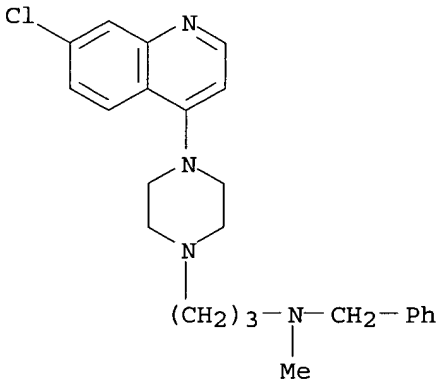
●2 HBr

RN 954-52-9 HCAPLUS
CN Quinoline, 7-chloro-4-(1-piperazinyl)-, dihydrochloride (8CI) (CA INDEX NAME)



● 2 HCl

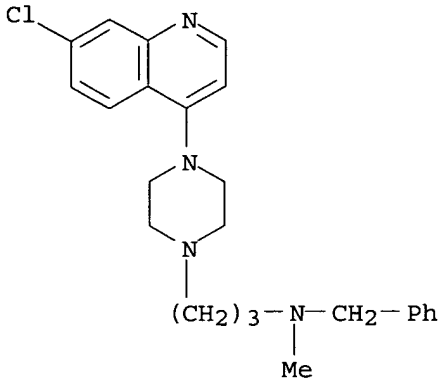
RN 1057-17-6 HCAPLUS
CN Quinoline, 4-[4-[3-(benzylmethylamino)propyl]-1-piperazinyl]-7-chloro-
(7CI, 8CI) (CA INDEX NAME)



RN 1063-52-1 HCAPLUS
CN Quinoline, 4-[4-[3-(benzylmethylamino)propyl]-1-piperazinyl]-7-chloro-,
maleate (1:3) (8CI) (CA INDEX NAME)

CM 1

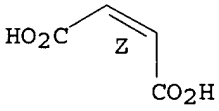
CRN 1057-17-6
CMF C24 H29 Cl N4



CM 2

CRN 110-16-7
CMF C4 H4 O4

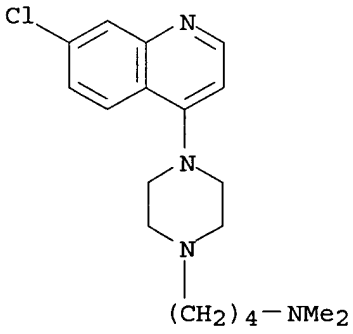
Double bond geometry as shown.



RN 1105-86-8 HCAPLUS
CN Quinoline, 7-chloro-4-[4-[4-(dimethylamino)butyl]-1-piperazinyl]-, maleate (1:3) (8CI) (CA INDEX NAME)

CM 1

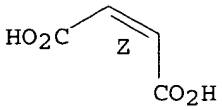
CRN 743-73-7
CMF C19 H27 Cl N4



CM 2

CRN 110-16-7
CMF C4 H4 O4

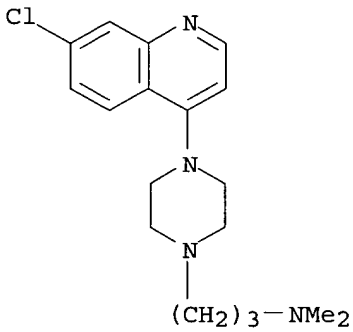
Double bond geometry as shown.



RN 1252-78-4 HCAPLUS
CN Quinoline, 7-chloro-4-[4-[3-(dimethylamino)propyl]-1-piperazinyl]-, maleate (1:3) (8CI) (CA INDEX NAME)

CM 1

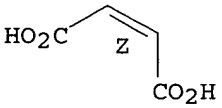
CRN 298-78-2
CMF C18 H25 Cl N4



CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



L76 ANSWER 18 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1964:440479 HCAPLUS
DOCUMENT NUMBER: 61:40479
ORIGINAL REFERENCE NO.: 61:7029h,7030a-d
TITLE: New quinolines
PATENT ASSIGNEE(S): Rhone-Poulenc S. A.
SOURCE: 33 pp.
DOCUMENT TYPE: **Patent**
LANGUAGE: Unavailable
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

BE 633453		19631210	BE	<--
DE 1197890			DE	
FR 1392458			FR	
GB 991838			GB	
PRIORITY APPLN. INFO.:			FR	19620614

GI For diagram(s), see printed CA Issue.

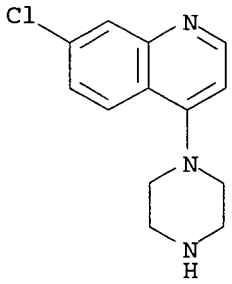
AB A mixture of 79.2 g. 4,7-dichloroquinoline (I), 42 g. 1,3-dipiperazinopropane (II), and 75.3 g. PhOH is heated in an oil-bath first at 110°, then at 140°, and finally 20 hrs. at 115-20°, and the reaction mixture poured into a hot solution of 40 g. NaOH in 500 ml. H2O to give 1,3-bis[1-(7-chloro-4-quinolyl)-4-piperazinyl] propane (III). III in 450 ml. HCONMe2 at 120-30° is treated with 5 g. C and filtered hot to give 59 g. III, m. 198-200°; III 7-MeO analog m. 18°. II, m. 125-7°, is prepared by condensation of 303 g. 1,3-dibromopropane with 474 g. 7-ethoxycarbonylpiperazine in the presence of Et2NH. Similarly prepared were the following IV (A and m.p. given): trans-1,4-cyclohexylenedimethylene, m. 276-9°; hexamethylene, m. 173°; pentamethylene, m. 161°; decamethylene, m. 119-21°; p-xylylene, m. 217-18°; ethylene, m. 228-30°; 3,3-dimethylpentamethylene, m. 177-8° tetramethylene, m.185-6°; trans-2-butenylene, m. 192-4°; 2-butynylene, m. 202-3°; nonamethylene, m. 115-16°. Also prepared are 1,3-bis[1-(6-chloro-4-quinolyl)-4-piperazinyl]propane, m. 70-80°, and 1,3-bis [1-(7-chloro-4-quinolyl)-trans-2,5-dimethyl- 4-piperazinyl] propane, m. 100°. A mixture of 13.5 g. [1-(7-chloro-4-quinolyl)-4-piperazinyl]-3-chloropropane, 10.3 g. 1-(6-chloro-4-quinolyl)piperazine, 6.2 g. NaI, and 4.16 g. Et3N in 125 ml. MeCOEt is refluxed 6 hrs. and poured into 500 ml. N NaOH and the mixture filtered, washed, and dried to give 11.3 g. 1-[1-(7-chloro-4-quinolyl)-4-piperazinyl]-3-[1-(6-chloro-4-quinolyl)-4-piperazinyl] propane, m. 95°. 1-[1-(7-Methoxy-4-quinolyl)-4-piperazinyl]-3-[1-(6-chloro-4-quinolyl)-4-piperazinyl]propane, m. 136-8°, is prepared from 1-(1-[7-methoxy-4-quinolyl)-4-piperazinyl]-3-chloropropane and 1-(6-chloro-4-quinolyl)piperazine.

IT **837-52-5**, Quinoline, 7-chloro-4-(1-piperazinyl)- **4039-02-5**, Quinoline, 4,4'-(2-butynylenedi-4,1-piperazinediyl)bis[7-chloro- **4085-31-8**, Quinoline, 4,4'-(trimethylenedi-4,1-piperazinediyl)bis[7-chloro- **4086-55-9**, Quinoline, 7-chloro-7'-methoxy-4,4'-(trimethylenedi-4,1-piperazinediyl)di- **4257-09-4**, Quinoline, 4,4'-(tetramethylenedi-4,1-piperazinediyl)bis[7-chloro- **4407-18-5**, Quinoline, 6,7'-dichloro-4,4'-(trimethylenedi-4,1-piperazinediyl)di- **4914-50-5**, Piperazine, 1-(7-chloro-4-quinolyl)-4-[4-[4-(7-chloro-4-quinolyl)-1-piperazinyl]butyryl]- **39844-41-2**, 1-Piperazineethanol, 4-(7-chloro-4-quinolyl)- **92645-66-4**, Quinoline, 7-chloro-4-[4-(2-chloroethyl)-1-piperazinyl]- **96264-32-3**, Quinoline, 4,4'-(ethylenedi-4,1-piperazinediyl)bis[7-chloro- **96588-60-2**, Quinoline, 4,4'-[(3,3-dimethylpentamethylene)di-4,1-piperazinediyl]bis[7-chloro- **96773-26-1**, Quinoline, 4,4'-(decamethylenedi-4,1-piperazinediyl)bis[7-chloro- **97154-81-9**, Quinoline, 4,4'-(2-butenylenedi-4,1-piperazinediyl)bis[7-chloro- **97433-01-7**, Quinoline, 4,4'-(pentamethylene-di-4,1-piperazinediyl)bis[7-chloro- **97615-56-0**, Quinoline, 4,4'-(nonamethylenedi-4,1-piperazinediyl)bis[7-chloro- **97615-66-2**, Quinoline, 4,4'-(hexamethylenedi-4,1-piperazinediyl)bis[7-chloro- **97656-31-0**, Quinoline, 7-chloro-4-[4-[p-[[4-(7-chloro-4-quinolyl)-1-piperazinyl]methyl]benzyl]-1-piperazinyl]- **98879-06-2**, Quinoline, 2,4'-[trimethylenebis(2,5-dimethyl-4,1-piperazinediyl)]bis[7-

chloro- **106172-91-2**, Quinoline, 7-chloro-4-[4-[4-[[4-(7-chloro-4-quinolyl)-1-piperazinyl]methyl]cyclohexyl]methyl]-1-piperazinyl]- (preparation of)

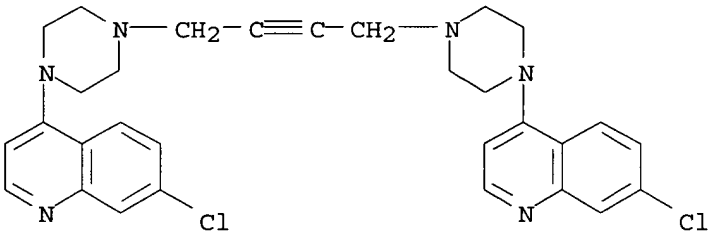
RN 837-52-5 HCAPLUS

CN Quinoline, 7-chloro-4-(1-piperazinyl)- (7CI, 8CI, 9CI) (CA INDEX NAME)



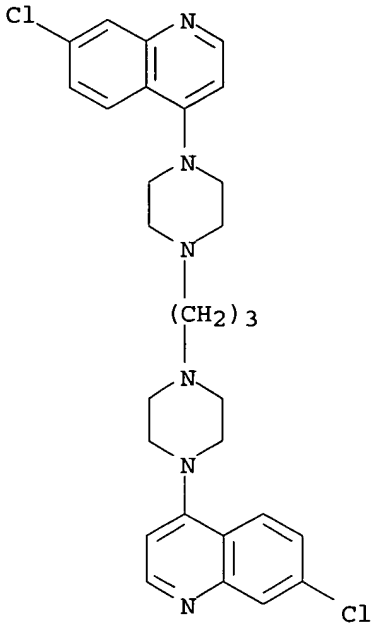
RN 4039-02-5 HCAPLUS

CN Quinoline, 4,4'-(2-butynylenedi-4,1-piperazinediyl)bis[7-chloro- (7CI, 8CI) (CA INDEX NAME)

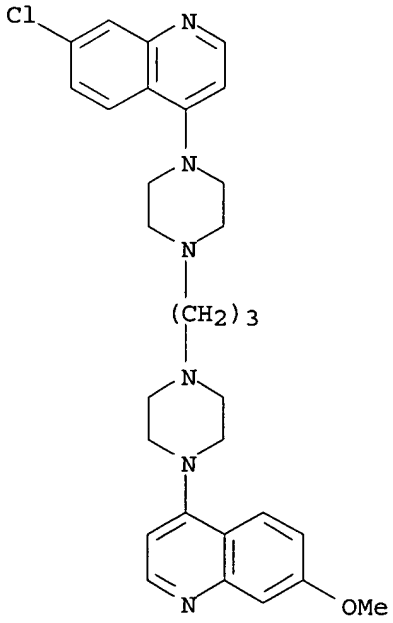


RN 4085-31-8 HCAPLUS

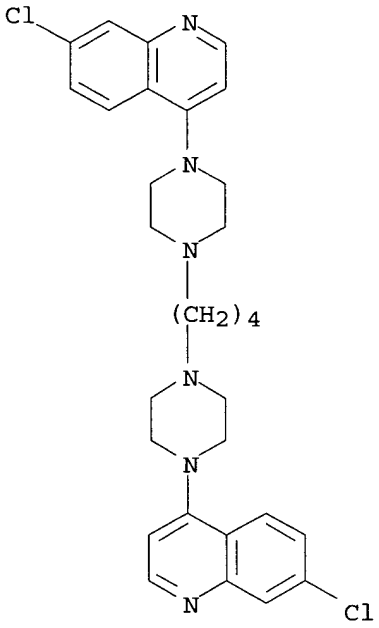
CN Quinoline, 4,4'-(1,3-propanediyldi-4,1-piperazinediyl)bis[7-chloro- (9CI) (CA INDEX NAME)



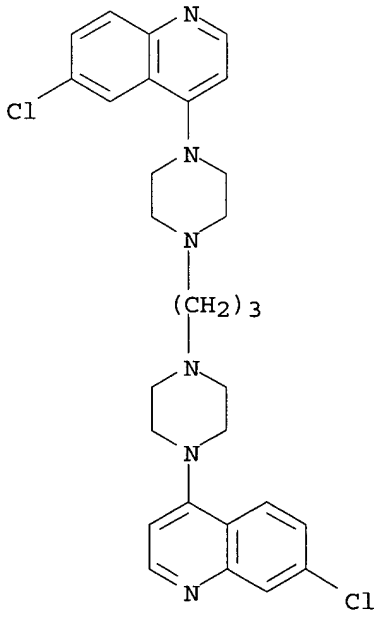
RN 4086-55-9 HCAPLUS
CN Quinoline, 7-chloro-7'-methoxy-4,4'-(trimethylenedi-4,1-piperazinediyl)di- (8CI) (CA INDEX NAME)



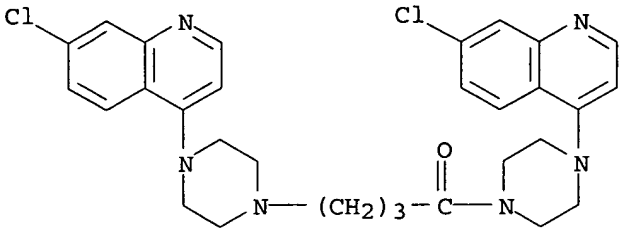
RN 4257-09-4 HCAPLUS
CN Quinoline, 4,4'-(tetramethylenedi-4,1-piperazinediyl)bis[7-chloro- (7CI, 8CI) (CA INDEX NAME)



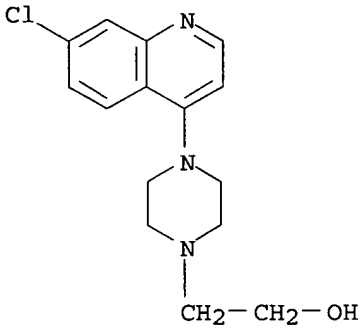
RN 4407-18-5 HCAPLUS
CN Quinoline, 6,7'-dichloro-4,4'-(trimethylenedi-4,1-piperazinediyl)di- (7CI, 8CI) (CA INDEX NAME)



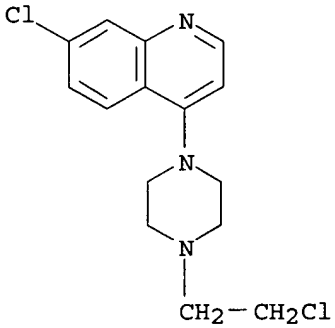
RN 4914-50-5 HCAPLUS
CN Piperazine, 1-(7-chloro-4-quinolyl)-4-[4-[4-(7-chloro-4-quinolyl)-1-piperazinyl]butyryl]- (7CI, 8CI) (CA INDEX NAME)



RN 39844-41-2 HCAPLUS
CN 1-Piperazineethanol, 4-(7-chloro-4-quinolinyl)- (9CI) (CA INDEX NAME)

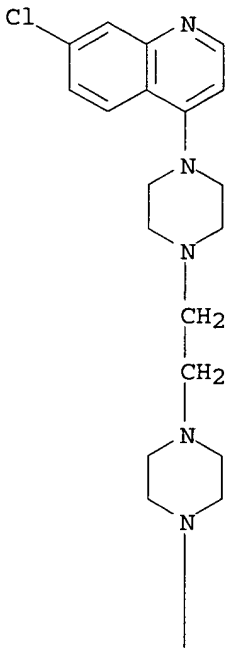


RN 92645-66-4 HCAPLUS
CN Quinoline, 7-chloro-4-[4-(2-chloroethyl)-1-piperazinyl]- (7CI) (CA INDEX NAME)

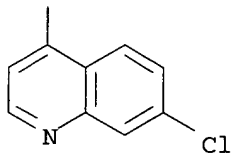


RN 96264-32-3 HCAPLUS
CN Quinoline, 4,4'-(ethylenedi-4,1-piperazinediyl)bis[7-chloro- (7CI) (CA INDEX NAME)

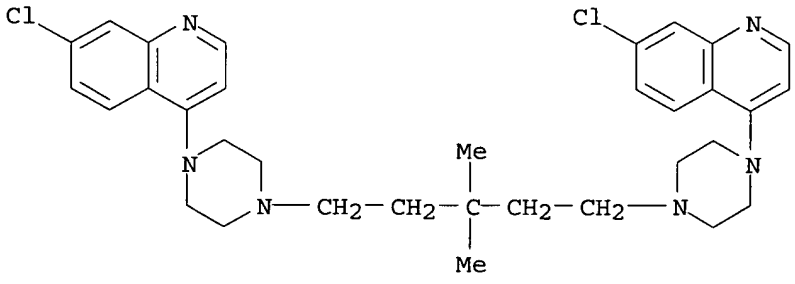
PAGE 1-A



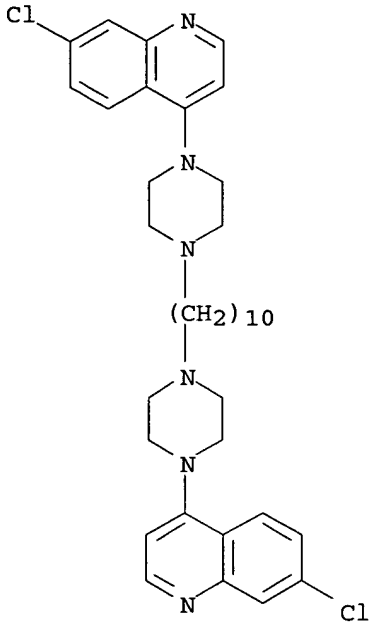
PAGE 2-A



RN 96588-60-2 HCAPLUS
CN Quinoline, 4,4'-[(3,3-dimethylpentamethylene)di-4,1-piperazinediyl]bis-[7-chloro- (7CI) (CA INDEX NAME)

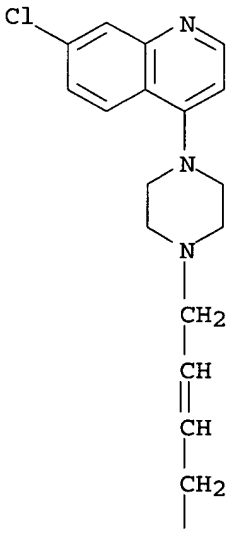


RN 96773-26-1 HCAPLUS
CN Quinoline, 4,4'-(decamethylenedi-4,1-piperazinediyl)bis[7-chloro- (7CI) (CA INDEX NAME)

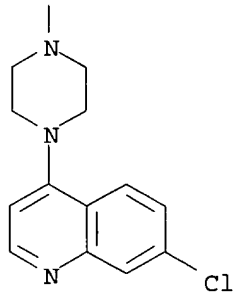


RN 97154-81-9 HCAPLUS
CN Quinoline, 4,4'-(2-butenylenedi-4,1-piperazinediyl)bis[7-chloro- (7CI) (CA INDEX NAME)

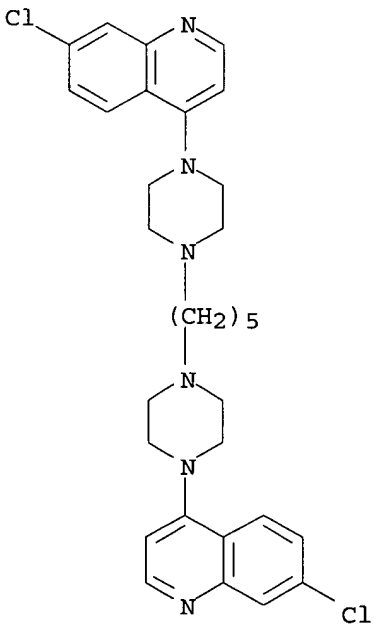
PAGE 1-A



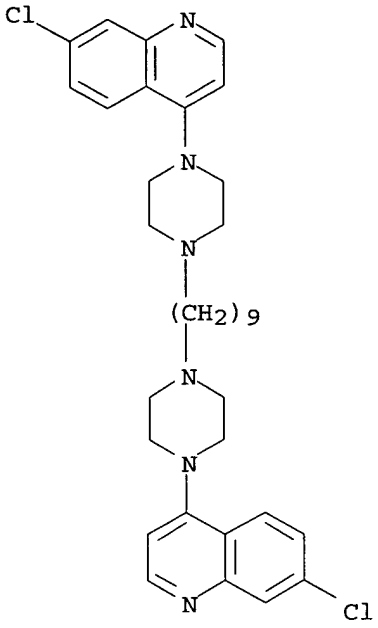
PAGE 2-A



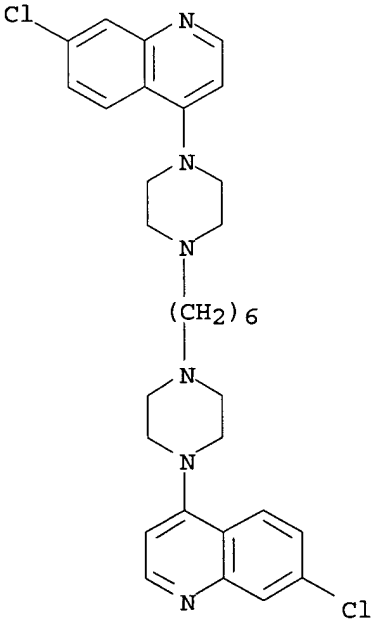
RN 97433-01-7 HCAPLUS
CN Quinoline, 4,4'-(pentamethylenedi-4,1-piperazinediyl)bis[7-chloro- (7CI) (CA INDEX NAME)



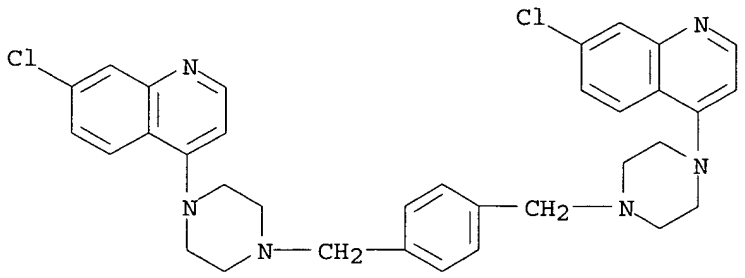
RN 97615-56-0 HCAPLUS
CN Quinoline, 4,4'-(nonamethylenedi-4,1-piperazinediyl)bis[7-chloro- (7CI) (CA INDEX NAME)



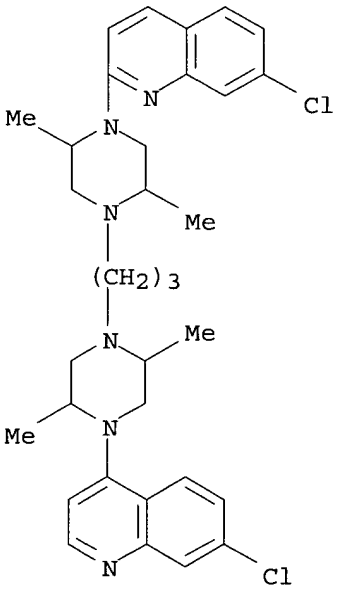
RN 97615-66-2 HCAPLUS
CN Quinoline, 4,4'-(hexamethylenedi-4,1-piperazinediyl)bis[7-chloro- (7CI) (CA INDEX NAME)



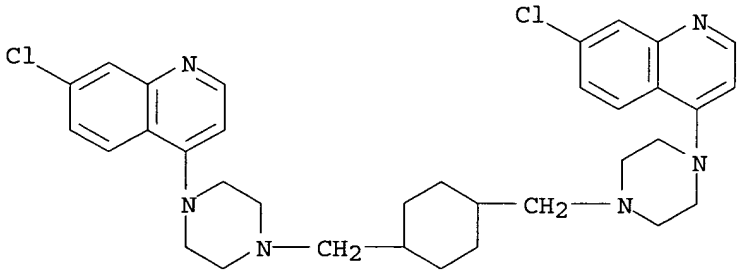
RN 97656-31-0 HCAPLUS
CN Quinoline, 7-chloro-4-[4-[p-[[4-(7-chloro-4-quinolyl)-1-piperazinyl]methyl]benzyl]-1-piperazinyl]- (7CI) (CA INDEX NAME)



RN 98879-06-2 HCAPLUS
CN Quinoline, 2,4'-[trimethylenebis(2,5-dimethyl-4,1-piperazinediyl)]bis[7-chloro- (7CI) (CA INDEX NAME)



RN 106172-91-2 HCAPLUS
CN Quinoline, 7-chloro-4-[4-[[4-[[4-(7-chloro-4-quinolyl)-1-piperazinyl]methyl]cyclohexyl]methyl]-1-piperazinyl]- (7CI) (CA INDEX NAME)



L76 ANSWER 19 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1964:425456 HCAPLUS
DOCUMENT NUMBER: 61:25456
ORIGINAL REFERENCE NO.: 61:4372h,4373a-b
TITLE: 1,4-Bis [(7-chloro-4-quinolylamino)alkyl] piperazine di- N-oxides
PATENT ASSIGNEE(S): Rhone-Poulenc SA
SOURCE: 7 pp.
DOCUMENT TYPE: **Patent**
LANGUAGE: Unavailable
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR M2371		19640331	FR	19621029 <--

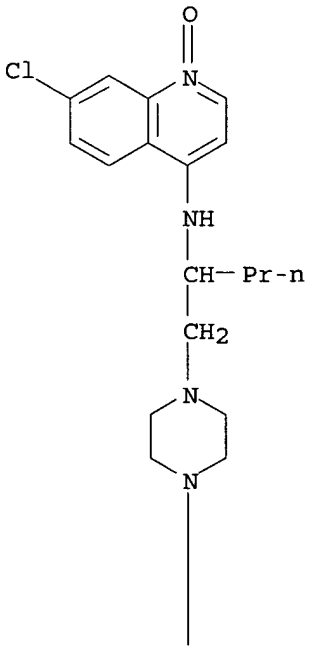
AB Piperazines are treated with H2O2 in HOAc to give the title compds. which can be used as antimalarial agents. Thus, 20 ml. H2O2 is added to a solution of 28.95 g. meso-1,4-bis[4-(7-chloro-4-quinolylamino)pentyl]piperazine in 250 ml. HOAc, and the mixture kept overnight, poured into 1500 ml. 4N NaOH, and filtered. The base is dissolved in 300 ml. EtOH, 57 ml. 4.6N HCl (ether) added, and the mixture filtered to give 36.4 g. meso-1,4-bis[4-(7-chloro-4-quinolylamino)pentyl]piperazine di-N-oxide-4HCl, m. .apprx.244°. Similarly prepared are (m.p. given): 1,4-bis[2-(7-chloro-4-quinolylamino)propyl]-piperazine di-N-oxide-4HCl, 254° and 1-[2-(7-chloro-4-quinolylamino)pentyl]-4-(7-chloro-4-quinolyl)piperazine di- N- oxide, 140°.

IT **101058-57-5**, Quinoline, 7-chloro-4-[4-[2-[(7-chloro-4-quinolyl)amino]pentyl]-1-piperazinyl]-, 1,4-dioxide
(preparation of)

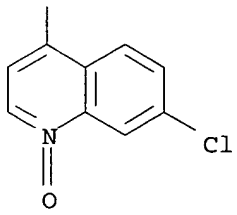
RN 101058-57-5 HCAPLUS

CN Quinoline, 7-chloro-4-[4-[2-[(7-chloro-4-quinolyl)amino]pentyl]-1-piperazinyl]-, 1,4-dioxide (7CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



L76 ANSWER 20 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1963:435548 HCAPLUS
DOCUMENT NUMBER: 59:35548
ORIGINAL REFERENCE NO.: 59:6370b-h
TITLE: 4-Aminoquinoline derivatives
PATENT ASSIGNEE(S): Rhone-Poulenc S. A.
SOURCE: 37 pp.
DOCUMENT TYPE: **Patent**
LANGUAGE: Unavailable
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
BE 618068		19621126	BE		<--
DE 1195319			DE		
FR 1343486			FR		
FR AD82059			FR		
FR AD82071			FR		
FR M1962			FR		
GB 1002187			GB		
US 3126384		1964	US		<--
PRIORITY APPLN. INFO.:			FR	19610526	

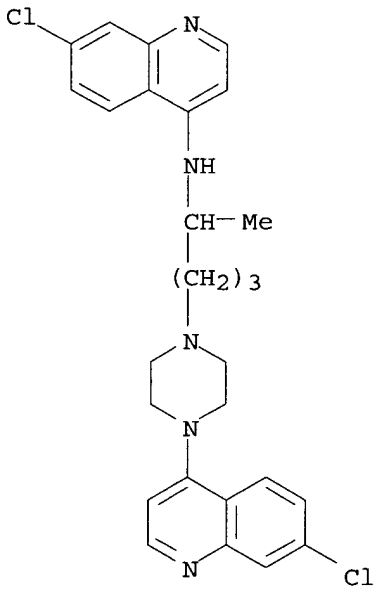
GI For diagram(s), see printed CA Issue.
AB The title compds. display antimalarial, anthelmintic, and amebicidal activity. A stirred mixture of 133 g. 4-(5-piperazino-2-pentyl)amino-7-chloroquinoline, 87 g. 4,7-dichloroquinoline, 720 g. phenol, and 2 g. NH4Cl is heated 4 hrs. at 180°, cooled, poured into 8 l. dilute NaOH solution, the solution extracted with 2 l. CHCl3, and the exts. worked up to yield
166 g. 1-[4-(7-chloro - 4 - quinolyl)aminopentyl] - 4-(7-chloro-4-quinolyl)piperazine, m. 125°; picrate, m. 200° (Me2NCHO); embonate m. 260°. Similarly are prepared the following I (X and m.p. given); CH2CH2 217-18°; CH2CH2CH2, 178-9°; CH2CMe2CH2, 224°; CHMeCH2CH2, 172-3°; (CH2)5, 168°; CH(Bu-iso)CH2, 153-4°; CH2CHMeCH2, 218-20°; (CH2)4, 173-5°; CHEtCH2, 177-8°; D(-)-CHMeCH2, 182-4°, [α]23D -180 ± 1°(c2,EtOH); L(+)CHMeCH2, 181-2° [α]23D 177 ± 1° (c 2, EtOH); DL-CHMeCH2, 194-5°.
The following II were prepared (Z and m.p. given): 6-chloro-4-quinolyl, 110°; 7-methoxy-4-quinolyl, 192° (monohydrate, 140°); 7-dimethylsulfamoyl-4-quinolyl, 120°; 7-trifluoromethyl-4-quinolyl, 90-100°; 3-methyl-7-chloro-4-quinolyl, 130°; 4-pyridyl, 191-2°; 2-amino-4-ethyl-5-(p-chlorophenyl)-6-pyrimidyl, 114-17°; 2-pyrimidyl, 143-4°; 2-(p-chlorophenyl4-methyl-6-

pyrimidyl, 106-10°; 2-amino-4-pyrimidyl, 191-3°; 2-methoxy-6-chloro-9-acridyl, 136-8°; 2-methyl-6-acetamidoquinolyl, 246°; 2-methyl-6-amino-4-quinolyl. 1-4-(6-Chloro-4-quinolyl)aminopentyl]-4-(7-chloro-4-quinolyl)piperazine, m. 110°, 1-[2-(7-chloro-4-quinolyl)aminopentyl]-4-(2-pyridyl)piperazine, m. 162-3°, 1-[2-(7-chloro-4-quinolyl)aminopentyl]-4-(2-phenyl-4-pyridyl)piperazine, m. 178-9°, and 1-[4-(7-chloro-4 quinolyl)aminopentyl]-4-(7-chloro-4-quinolyl)hexahydro-1,4-diazepine oxalate, m. 185°, were also prepared The preparation of the following compds. (required as intermediates in the preparation of the above) was given: 1-phthalimido-5-bromopentane, m. 61-2°; 1-(5-phthalimidopentyl)-4-ethoxycarbonylpiperazine, m. 196-8°; 1-(5-aminopentyl)piperazine; 1-(3-aminobutyl)-4-ethoxycarbonylpiperazine, b0.5 134-5°; 1-[3-(7-chloro-4-quinolyl)aminobutyl]-4-ethoxycarbonylpiperazine picrate, m. 263-9°; 4-(4-piperazine-2-butyl)amino-7-chloroquinoline, m. 196-7°; 1-benzyl-4-(1-cyanoethyl)piperazine, b0.5 155-9°; 1-benzyl-4-(1methyl-2-aminoethyl)piperazine, b0.5 132-5°; D(-)-alaninol, b10 68-9°, [α]25D -23 ± 1° (c 2, EtOH); L(+)-alaninol, b24 85 8°, [α]22D 20.7 ± 0.8° (c 2.2, EtOH); D(-)-4-(3-hydroxy-2propyl)amino-7-chloroquinoline, m. 223-4°, [α]25D -29.4 ± 2° (c 1.2, EtOH), and the L(+)-epimer, m. 224-6°, [α]22D 30 ± 2° (c 1, EtOH); D(-)-4-(3-chloro-2-propyl)amino-7-chloroquinoline, m. 146-7°, [α]24D -103.5 ± 1° (c 2, EtOH), and the L(+)-epimer, m. 146-8°, [α]2D2 100 ± 1° (c 2, EtOH); D(-)-4-(3-piperazino-2-propyl)amino-7-chloroquinoline, m. 131-2°, [α]2D3 137 ± 1° (c 2, EtOH), and the L(+)-epimer, m. 128-30°, [α]2D4 140 ± 2° (c 2, EtOH); 4-(5'-hydroxy-2'-pentyl)-6-chloroquinoline, m. 142° (the 5'-chloro analog, m. 156°, and the 5'-piperazine analog, m. 90°); 2-hydroxymethylpropylamine, b. 182-4.5°; 4-(2-hydroxy-methylpropylamino)-7-chloroquinoline, m. 156-8°; 4-(2-chloromethylpropylamino)-7-chloroquinoline, m. 141-3°; 4-(3-piperazino-2-methylpropylamino)-7-chloroquinoline, m. 159-60°; 4-(4-piperazinobutylmino)-7-chloroquinoline, m. 140-2°; 4-(2'hydroxy-1'-isobutylethylamino)-7-chloroquinoline, m. 168-9°, the 2'-chloro analog, m. 148-9°, and the 2'-piperazine analog, m. 178-80°; 4-(5-hydroxy-2-pentyl)(acetyl)amino-7-chloroquinoline, m. 107-8°; 1-(3-aminopropyl)-4-(7-chloro-4-quinolyl)-piperazine; 1-[4-(7-chloro-4-quinolyl)aminopentyl] hexahydro-1,4-diazepine.

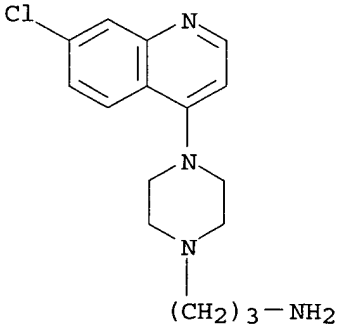
IT **10547-39-4**, Quinoline, 7-chloro-4-[4-[4-[(7-chloro-4-quinolyl)amino]pentyl]-1-piperazinyl]- **94163-65-2**, Quinoline, 4-[4-(3-aminopropyl)-1-piperazinyl]-7-chloro- **95560-84-2**, Quinoline, 7-chloro-4-[4-[2-[(7-chloro-4-quinolyl)amino]ethyl]-1-piperazinyl]- **95802-53-2**, Quinoline, 7-chloro-4-[4-[3-[(7-chloro-4-quinolyl)amino]propyl]-1-piperazinyl]- **96771-07-2**, Quinoline, 7-chloro-4-[4-[2-[(7-chloro-4-quinolyl)amino]butyl]-1-piperazinyl]- **96771-08-3**, Quinoline, 7-chloro-4-[4-[3-[(7-chloro-4-quinolyl)amino]butyl]-1-piperazinyl]- **96771-09-4**, Quinoline, 7-chloro-4-[4-[4-[(7-chloro-4-quinolyl)amino]butyl]-1-piperazinyl]- **96771-10-7**, Quinoline, 7-chloro-4-[4-[3-[(7-chloro-4-quinolyl)amino]-2-methylpropyl]-1-piperazinyl]- **96809-38-0**, Quinoline, 7-chloro-4-[4-[2-[(7-chloro-4-quinolyl)amino]-1-methylpentyl]-1-piperazinyl]- **98588-41-1**, Quinoline, 7-chloro-4-[4-[4-[(6-chloro-4-quinolyl)amino]-1-methylbutyl]-1-piperazinyl]- **98588-43-3**, Quinoline, 7-chloro-4-[4-[5-[(7-chloro-4-quinolyl)amino]pentyl]-1-piperazinyl]- **99166-73-1**, Quinoline, 7-chloro-4-[4-[3-[(7-chloro-4-quinolyl)amino]-2,2-dimethylpropyl]-1-piperazinyl]- **856580-95-5**, Quinoline, 7-chloro-4-[4-[4-[(7-chloro-4-quinolyl)amino]pentyl]-1-piperazinyl]-, compound with 4,4'-methylenebis[3-hydroxy-2-naphthoic acid]

856602-02-3, Quinoline, 7-chloro-4-[4-[4-[(7-chloro-4-quinolyl)amino]pentyl]-1-piperazinyl]-3-methyl- **856602-05-6**, Quinoline, 7-chloro-4-[4-[4-[(7-chloro-4-quinolyl)amino]pentyl]-1-piperazinyl]-, picrate
(preparation of)

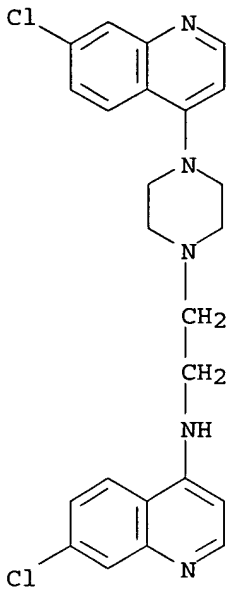
RN 10547-39-4 HCAPLUS
CN Quinoline, 7-chloro-4-[4-[4-[(7-chloro-4-quinolyl)amino]pentyl]-1-piperazinyl]- (7CI, 8CI) (CA INDEX NAME)



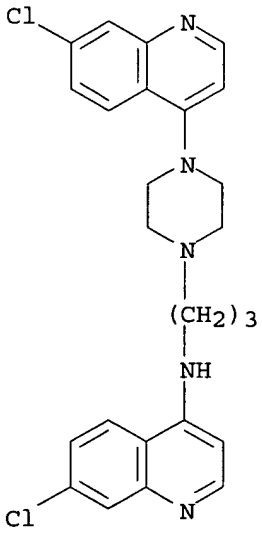
RN 94163-65-2 HCAPLUS
CN Quinoline, 4-[4-(3-aminopropyl)-1-piperazinyl]-7-chloro- (7CI) (CA INDEX NAME)



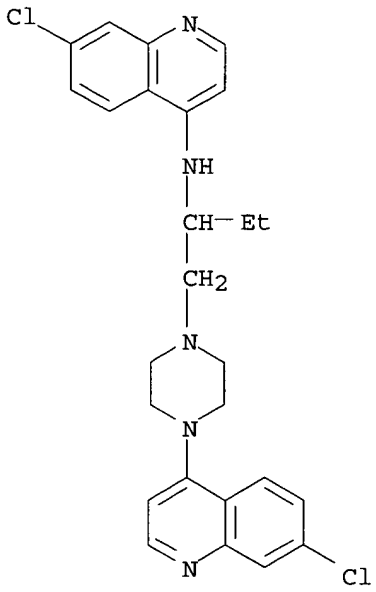
RN 95560-84-2 HCAPLUS
CN 4-Quinolinamine, 7-chloro-N-[2-[4-(7-chloro-4-quinolinyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



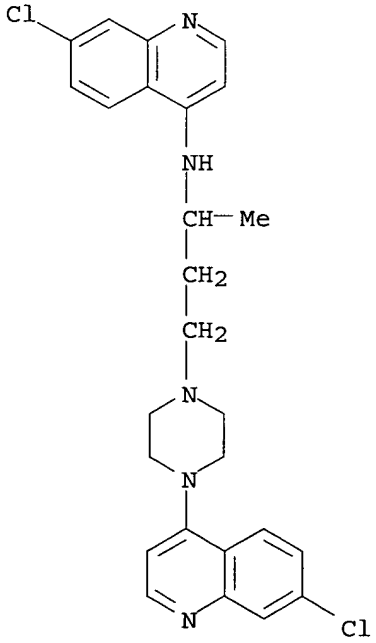
RN 95802-53-2 HCAPLUS
CN Quinoline, 7-chloro-4-[4-[3-[(7-chloro-4-quinolyl)amino]propyl]-1-piperazinyl]- (7CI) (CA INDEX NAME)



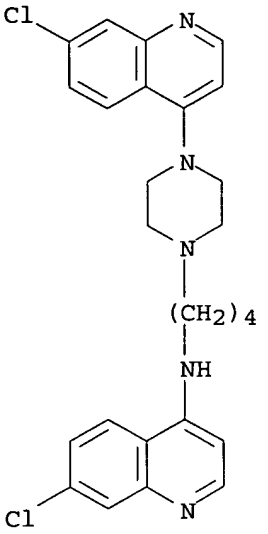
RN 96771-07-2 HCAPLUS
CN Quinoline, 7-chloro-4-[4-[2-[(7-chloro-4-quinolyl)amino]butyl]-1-piperazinyl]- (7CI) (CA INDEX NAME)



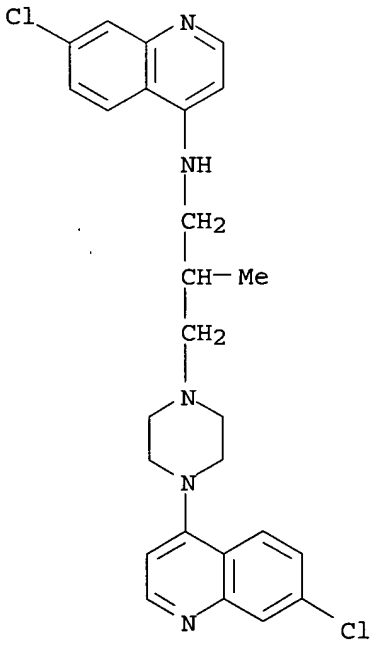
RN 96771-08-3 HCAPLUS
CN Quinoline, 7-chloro-4-[4-[3-[(7-chloro-4-quinolyl)amino]butyl]-1-piperazinyl]- (7CI) (CA INDEX NAME)



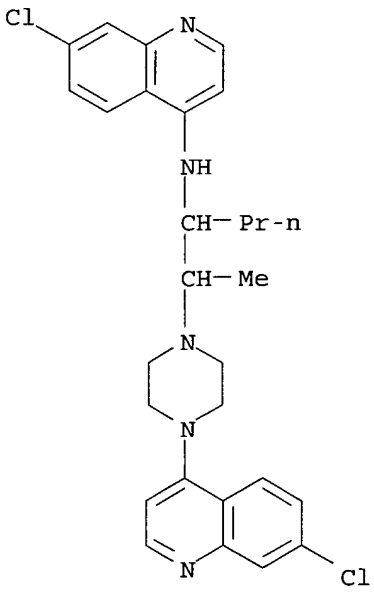
RN 96771-09-4 HCAPLUS
CN Quinoline, 7-chloro-4-[4-[4-[(7-chloro-4-quinolyl)amino]butyl]-1-piperazinyl]- (7CI) (CA INDEX NAME)



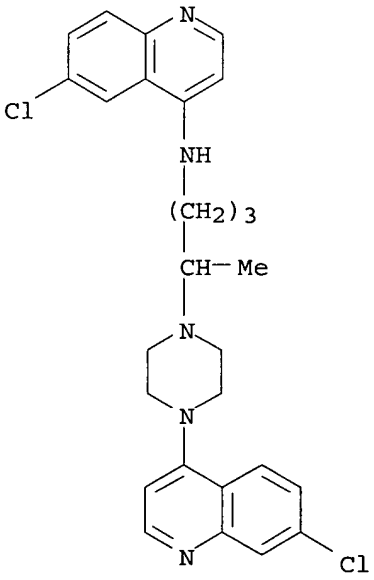
RN 96771-10-7 HCAPLUS
CN Quinoline, 7-chloro-4-[4-[3-[(7-chloro-4-quinolyl)amino]-2-methylpropyl]-1-piperazinyl]- (7CI) (CA INDEX NAME)



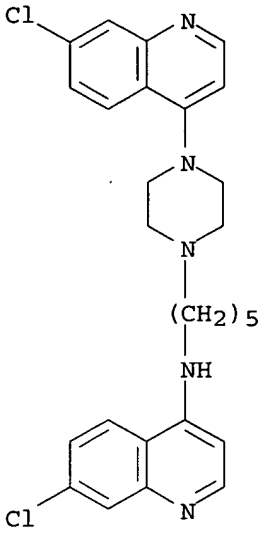
RN 96809-38-0 HCAPLUS
CN Quinoline, 7-chloro-4-[4-[2-[(7-chloro-4-quinolyl)amino]-1-methylpentyl]-1-piperazinyl]- (7CI) (CA INDEX NAME)



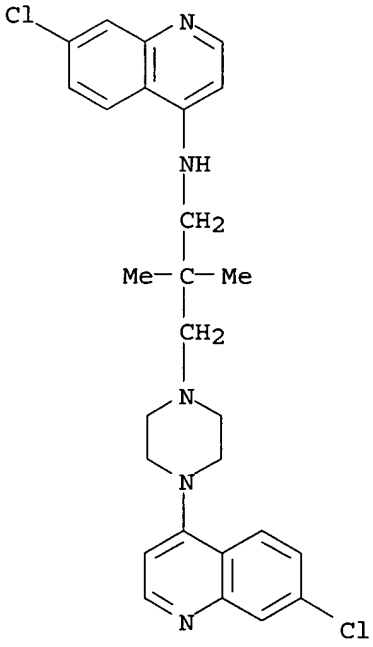
RN 98588-41-1 HCAPLUS
CN Quinoline, 7-chloro-4-[4-[4-[(6-chloro-4-quinolyl)amino]-1-methylbutyl]-1-piperazinyl]- (7CI) (CA INDEX NAME)



RN 98588-43-3 HCAPLUS
CN Quinoline, 7-chloro-4-[4-[5-[(7-chloro-4-quinolyl)amino]pentyl]-1-piperazinyl]- (7CI) (CA INDEX NAME)



RN 99166-73-1 HCAPLUS
CN Quinoline, 7-chloro-4-[4-[3-[(7-chloro-4-quinolyl)amino]-2,2-dimethylpropyl]-1-piperazinyl]- (7CI) (CA INDEX NAME)

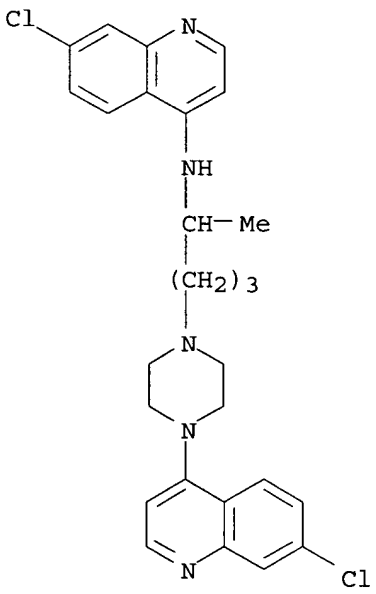


RN 856580-95-5 HCAPLUS
CN Quinoline, 7-chloro-4-[4-[4-[(7-chloro-4-quinolyl)amino]pentyl]-1-piperazinyl]-, compd. with 4,4'-methylenebis[3-hydroxy-2-naphthoic acid] (7CI) (CA INDEX NAME)

CM 1

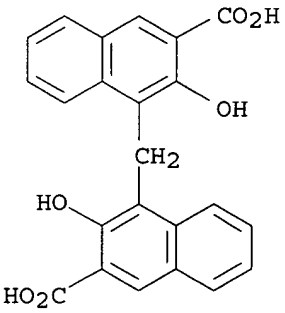
CRN 10547-39-4

CMF C27 H29 Cl2 N5

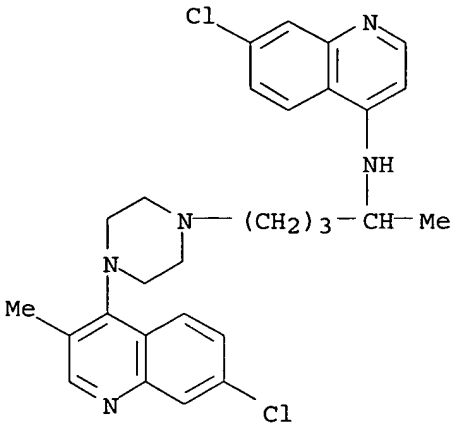


CM 2

CRN 130-85-8
CMF C23 H16 O6



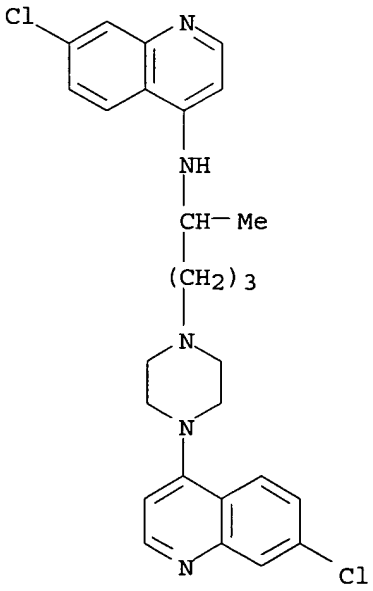
RN 856602-02-3 HCAPLUS
CN Quinoline, 7-chloro-4-[4-[4-[(7-chloro-4-quinolyl)amino]pentyl]-1-piperazinyl]-3-methyl- (7CI) (CA INDEX NAME)



RN 856602-05-6 HCAPLUS
CN Quinoline, 7-chloro-4-[4-[4-[(7-chloro-4-quinolyl)amino]pentyl]-1-piperazinyl]-, picrate (7CI) (CA INDEX NAME)

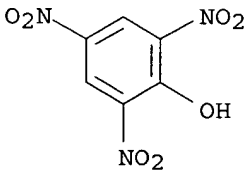
CM 1

CRN 10547-39-4
CMF C27 H29 Cl2 N5



CM 2

CRN 88-89-1
CMF C6 H3 N3 O7



```
=> => d stat que nos l77
L66             STR
L68         601 SEA FILE=REGISTRY SSS FUL L66
L69             STR
L70          12 SEA FILE=REGISTRY SUB=L68 SSS FUL L69
L71           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L70
L72         589 SEA FILE=REGISTRY ABB=ON  PLU=ON  L68 NOT L70
L73         102 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L72
L74          86 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L73 AND PD=<OCTOBER 24, 2003
L75          86 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L74 NOT L71
L76          20 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L75 AND PATENT/DT
L77          66 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L75 NOT L76


=> d ibib abs hitrn l77 1-66

L77  ANSWER 1 OF 66  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2003:816391  HCAPLUS
DOCUMENT NUMBER:          140:192272
TITLE:                    Comparative clinical trial of two-fixed combinations
                          dihydroartemisinin-naphthoquine-trimethoprim (DNP) and
                          artemether-lumefantrine (Coartem / Riamet) in the
                          treatment of acute uncomplicated falciparum malaria in
                          Thailand
AUTHOR(S):                Krudsood, S.; Chalermrut, K.; Pengruksa, C.;
                          Srivilairit, S.; Silachamroon, U.; Treeprasertsuk, S.;
                          Kano, S.; Brittenham, G. M.; Looareesuwan, S.
CORPORATE SOURCE:         Department of Tropical Hygiene, Faculty of Tropical
                          Medicine, Mahidol University, Bangkok, 10400, Thailand
SOURCE:                   Southeast Asian Journal of Tropical Medicine and
                          Public Health (2003), 34(2), 316-321
                          CODEN: SJTMAK; ISSN: 0125-1562
PUBLISHER:                SEAMEO-TROPMED Network
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   An open randomized comparison of two-fixed dose artemisinin
derivative-containing
     combination regimens was conducted in adults with acute uncomplicated
     multidrug resistant falciparum malaria in Thailand.  DNP, a combination of
     dihydroartemisinin with naphthoquine and trimethoprim developed recently
     in China, has been evaluated in China, Vietnam, Cambodia and Thailand.
     This study was performed to compare the safety, tolerability and efficacy
     of DNP and artemether-lumefantrine/ Coartem.  One hundred and thirty
     eligible uncomplicated falciparum malaria patients were enrolled into the
     study.  Patients were randomly assigned in a 2:1 ratio into group A, which
     received DNP one tablet twice a day for one day; and group B, which
     received Coartem/ Riamet four tablets twice a day for 3 days.  The cure
     rates at 28-day were 99% and 97% in group A and group B, resp.  No serious
     adverse events occurred.  We concluded that both DNP and Coartem/ Riamet
```

were safe, well tolerated and highly efficacious in the treatment of acute uncomplicated falciparum malaria in Thailand.

IT **509149-21-7**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(two-fixed combinations dihydroartemisinin-naphthoquine-trimethoprim (DNP) and artemether-lumefantrine (Coartem / Riamet) in treatment of acute falciparum malaria)

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 2 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:802815 HCAPLUS
DOCUMENT NUMBER: 140:22645
TITLE: Potent and Selective Inhibitors of Platelet-Derived Growth Factor Receptor Phosphorylation. 3. Replacement of Quinazoline Moiety and Improvement of Metabolic Polymorphism of 4-[4-(N-Substituted (thio)carbamoyl)-1-piperazinyl]-6,7-dimethoxyquinazoline Derivatives
AUTHOR(S): Matsuno, Kenji; Ushiki, Junko; Seishi, Takashi; Ichimura, Michio; Giese, Neill A.; Yu, Jin-Chen; Takahashi, Shusuke; Oda, Shoji; Nomoto, Yuji
CORPORATE SOURCE: Pharmaceutical Research Institute, Kyowa Hakko Kogyo Co., Ltd., Nagaizumi, Shizuoka, 411-8731, Japan
SOURCE: Journal of Medicinal Chemistry (**2003**), 46(23), 4910-4925
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:22645

AB We have previously reported that a series of 4-[4-(N-substituted (thio)carbamoyl)-1-piperazinyl]-6,7-dimethoxyquinazoline derivs. were potent and selective inhibitors of platelet-derived growth factor receptor (PDGFR) phosphorylation and demonstrated several biol. effects such as suppression of neointima formation following balloon injury in rat carotid artery by oral administration. Here, we investigated structure-activity relationships of the 6,7-dimethoxyquinazolinyl moiety. In regard to 6,7-dimethoxy groups, ethoxy analogs showed potent activity (IC50 of 16b is 0.04 μM; IC50 of 17a is 0.01 μM) and further extension of the alkyl group reduced activity. Interestingly, methoxyethoxy (IC50 of 16j is 0.02 μM; IC50 of 17h is 0.01 μM) and ethoxyethoxy (IC50 of 17j is 0.02 μM) analogs showed the most potent activity, suggesting that the inserted oxygen atom significantly interacts with β-PDGFR. Among tricyclic quinazoline derivs., the 2-oxoimidazo[4,5-e]quinazoline derivative 21a showed potent activity (IC50 = 0.10 μM). Regarding replacements of quinazoline by other heterocyclic rings, pyrazolo[3,4-d]pyrimidine (39a, IC50 = 0.17 μM) and quinoline (IC50 of 40a is 0.18 μM; IC50 of 40b is 0.09 μM) derivs. showed potent activity. Isoquinoline and some pyridopyrimidine derivs. were completely inactive; therefore, 1-aza has an important role. Also 7-aza and 8-aza substitution on the parent quinazoline ring has a detrimental effect on the interaction with β-PDGFR. We also demonstrated that the substituents on the quinazoline ring possess major consequences for metabolic polymorphism. Although there existed extensive metabolizers and poor metabolizers in Sprague-Dawley rats administered 6,7-dimethoxyquinazoline derivs. (1b and 1c), 6-(2-methoxy)ethoxy-7-methoxyquinazoline analog 16k showed no metabolic polymorphism.

IT **205255-54-5P 205258-54-4P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and structure activity relationships of methoxyquinazoline derivs. as inhibitors of PDGFR phosphorylation)
IT **837-52-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and structure activity relationships of methoxyquinazoline derivs. as inhibitors of PDGFR phosphorylation)
REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 3 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:752477 HCAPLUS
DOCUMENT NUMBER: 140:228324
TITLE: Automated Solid-Phase Extraction Method for the Determination of Piperaquine in Whole Blood by Rapid Liquid Chromatography
AUTHOR(S): Lindegardh, N.; Ashton, M.; Bergqvist, Y.
CORPORATE SOURCE: Dalarna University College, Borlaenge, 781 88, Swed.
SOURCE: Therapeutic Drug Monitoring (**2003**), 25(5), 544-551
CODEN: TDMODV; ISSN: 0163-4356
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A bioanalytic method for the determination of piperaquine in whole blood by solid-phase extraction and rapid liquid chromatog. has been developed and validated. Whole blood was hemolyzed with deionized water, and an internal standard was added to the samples before they were loaded onto a PRS cation-exchange solid-phase extraction column. Piperaquine and internal standard
were analyzed by liquid chromatog. on a Chromolith Performance (100 + 4.6 mm) column with mobile phase acetonitrile:phosphate buffer, I = 0.1, pH 2.5 (8:92, volume/volume), flow rate 4 mL + min-1, and UV detection at 345 nm. The intra-assay precision for whole blood was 3.2% at 3.00 μM and 12.3% at 0.100 μM. The inter-assay precision for whole blood was 1.8% at 3.00 μM and 5.2% at 0.100 μM. The lower limit of quantification and the limit of detection were 0.050 μM and 0.010 μM, resp.
IT **4085-31-8**, Piperaquine
RL: ANT (Analyte); PKT (Pharmacokinetics); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(automated solid-phase extraction method for the determination of piperaquine in
whole blood by rapid liquid chromatog.)
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 4 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:741726 HCAPLUS
DOCUMENT NUMBER: 140:24370
TITLE: Novel small molecule inhibitors of botulinum neurotoxin A metalloprotease activity
AUTHOR(S): Burnett, James C.; Schmidt, James J.; Stafford, Robert G.; Panchal, Rekha G.; Nguyen, Tam L.; Hermone, Ann R.; Vennerstrom, Jonathan L.; McGrath, Connor F.; Lane, Douglas J.; Sausville, Edward A.; Zaharevitz, Daniel W.; Gussio, Rick; Bavari, Sina
CORPORATE SOURCE: Developmental Therapeutics Program, NCI Frederick,

Frederick, MD, 21702, USA
SOURCE: Biochemical and Biophysical Research Communications (**2003**), 310(1), 84-93
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Botulinum neurotoxins (BoNTs) are among the most lethal biol. substances to have been weaponized and are listed as biodefense category A agents. Currently, no small mol. (non-peptidic) therapeutics exist to counter this threat; hence, identifying and developing compds. that inhibit BoNTs is a high priority. In the present study, a high-throughput assay was used to identify small mols. that inhibit the metalloprotease activity of BoNT serotype A light chain (BoNT/A LC). All inhibitors were further verified using a HPLC-based assay. Conformational analyses of these compds., in conjunction with mol. docking studies, were used to predict structural features that contribute to inhibitor binding and potency. Based on these results, a common pharmacophore for BoNT/A LC inhibitors is proposed. This is the first study to report small mols. (non-peptidics) that inhibit BoNT/A LC metalloprotease activity in the low μM range.
IT **95560-84-2**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel small mol. inhibitors of botulinum neurotoxin A metalloprotease activity)
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 5 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:728108 HCAPLUS
DOCUMENT NUMBER: 140:192195
TITLE: Synthesis of totarol amino alcohol derivatives and their antiplasmodial activity and cytotoxicity
AUTHOR(S): Clarkson, Cailean; Musonda, Chitalu C.; Chibale, Kelly; Campbell, William E.; Smith, Peter
CORPORATE SOURCE: Groote Schuur Hospital, Department of Medicine, Division of Pharmacology, University of Cape Town, Observatory, 7925, S. Afr.
SOURCE: Bioorganic & Medicinal Chemistry (**2003**), 11(20), 4417-4422
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The previously unknown antiplasmodial activity of the plant derived natural product totarol is reported. Novel β-amino alc. derivs. based on this natural product were designed, synthesized and evaluated for in vitro antiplasmodial activity and cytotoxicity. These derivs. showed antiplasmodial IC50 values in the range of 0.6-3.0 μM and were equally active against a chloroquine-sensitive and resistant strain of Plasmodium falciparum, while showing little cytotoxicity against a mammalian cell line (CHO). In terms of lead development, two of the compds. based on substituted phenylpiperazine warrant further investigation as potential antiplasmodial leads. In addition to their selective antiplasmodial activity and lack of chloroquine cross-resistance, these compds. are structurally different to any of the available antimalarial drugs.
IT **660834-27-5P**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(synthesis of totarol amino alc. derivs. and their antiplasmodial activity and cytotoxicity)

IT **837-52-5**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synthesis of totarol amino alc. derivs. and their antiplasmodial activity and cytotoxicity)

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 6 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:427788 HCAPLUS
DOCUMENT NUMBER: 139:285552
TITLE: Measurement of piperaquine in plasma by liquid chromatography with ultraviolet absorbance detection
AUTHOR(S): Hung, Te-Yu; Davis, Timothy M. E.; Ilett, Kenneth F.
CORPORATE SOURCE: School of Medicine and Pharmacology, The University of Western Australia, Crawley, 6009, Australia
SOURCE: Journal of Chromatography, B: Analytical Technologies in the Biomedical and Life Sciences (**2003**), 791(1-2), 93-101
CODEN: JCBAAI; ISSN: 1570-0232
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Piperaquine (PQ) is an antimalarial drug enjoying a resurgence of use in combination with an artemisinin derivative because of parasite resistance to standard treatments. Its pharmacokinetic properties have not been characterized. An assay for PQ in plasma was developed using solvent extraction and liquid chromatog. separation on a Waters XTerra RP18 column, with a mobile phase of 7% acetonitrile in water (containing 0.025% trifluoroacetic acid, 0.1% NaCl, and 0.008% triethylamine) and UV detection at 340 nm. The assay was linear up to 1000 μg/L. Intra- and interday relative standard deviations were <10% (5-500 μg/L) and <21% (5-500 μg/L), resp. Interday limits of quantitation and detection were 5 and 3 μg/L, resp. A preliminary pharmacokinetic study in a patient who received 2.56 g PQ phosphate orally with dihydroartemisinin as 4 doses over 32 h found an apparent steady-state volume of distribution of 447 L/kg, an apparent oral clearance 0.93 L/h/kg, and a terminal half-life of 17.3 days.

IT **4085-31-8**, Piperaquine
RL: ANT (Analyte); PKT (Pharmacokinetics); ANST (Analytical study); BIOL (Biological study)
(piperaquine determination in blood plasma of humans by HPLC with UV detection)

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 7 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:280511 HCAPLUS
DOCUMENT NUMBER: 139:17166
TITLE: In vitro activities of piperaquine and other 4-aminoquinolines against clinical isolates of Plasmodium falciparum in Cameroon
AUTHOR(S): Basco, Leonardo K.; Ringwald, Pascal
CORPORATE SOURCE: Institut de Recherche pour le Developpement (IRD)-Laboratoire de Recherche sur le Paludisme, Organisation de Coordination pour la lutte contre les Endemies en Afrique Centrale (OCEAC), Unite de

Recherche "Paludologie Afro-tropicale", Yaounde, Cameroon
SOURCE: Antimicrobial Agents and Chemotherapy (**2003**), 47(4), 1391-1394
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The spread of chloroquine-resistant Plasmodium falciparum calls for a constant search for new drugs. The in vitro activity of piperaquine, a new Chinese synthetic drug belonging to the bisquinolines, was evaluated in 103 fresh clin. isolates of P. falciparum in Cameroon, Central Africa, and compared with that of other 4-aminoquinoline and Mannich base derivs. and dihydroartemisinin. Piperaquine was highly active (geometric mean 50% inhibitory concentration, 38.9 nmol/L; range, 7.76 to 78.3 nmol/L) and equally active ($P > 0.05$) against the chloroquine-sensitive and the chloroquine-resistant isolates. There was a significant but low correlation of response between chloroquine and piperaquine ($r = 0.257$, $P < 0.05$). These results suggest that further development of piperaquine, in combination with dihydroartemisinin, holds promise for use in chloroquine-resistant regions of endemicity.
IT **4085-31-8**, Piperaquine
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in vitro activities of piperaquine and other aminoquinolines against clin. isolates of Plasmodium falciparum in Cameroon)
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 8 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:100103 HCAPLUS
DOCUMENT NUMBER: 138:297135
TITLE: An open randomized clinical trial of Artecom VS artesunate-mefloquine in the treatment of acute uncomplicated falciparum malaria in Thailand
AUTHOR(S): Wilairatana, P.; Krudsood, S.; Chalermrut, K.; Pengruksa, C.; Srivilairit, S.; Silachamroon, U.; Treeprasertsuk, S.; Looareesuwan, S.
CORPORATE SOURCE: Hospital for Tropical Diseases, Faculty of Tropical Medicine, Mahidol University, Thailand
SOURCE: Southeast Asian Journal of Tropical Medicine and Public Health (**2002**), 33(3), 519-524
CODEN: SJTMAK; ISSN: 0125-1562
PUBLISHER: SEAMEO-TROPMED Network
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The efficacy and safety of Artecom were assessed in an open randomized trial in adults presenting with acute, uncomplicated Plasmodium falciparum malaria in Thailand. Three hundred and fifty-two patients were randomly enrolled at the ratio of 2:1 into group A:B and received Artecom (group A) and the standard combination of artesunate and mefloquine (group B) resp. All patients had rapid initial clin. and parasitol. responses. There were no significant differences in fever clearance time and parasite clearance time between the two groups. The 28-day cure rates were high as 97% in both groups. Artecom was effective and well-tolerated as artesunate-mefloquine, the current treatment in this area of multidrug-resistant P. falciparum malaria.
IT **509149-21-7**, Artecom
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(Artecom vs. artesunate and mefloquine combination in treatment of acute uncomplicated falciparum malaria patients)
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 9 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:98418 HCAPLUS
DOCUMENT NUMBER: 139:223578
TITLE: Automated solid-phase extraction method for the determination of piperaquine in plasma by peak compression liquid chromatography
AUTHOR(S): Lindegardh, N.; Ashton, M.; Bergqvist, Y.
CORPORATE SOURCE: Dalarna University College, Borlange, 781 88, Swed.
SOURCE: Journal of Chromatographic Science (**2003**), 41(1), 44-49
CODEN: JCHSBZ; ISSN: 0021-9665
PUBLISHER: Preston Publications
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A validated bioanal. method for the determination of piperaquine (PQ) in plasma by solid-phase extraction (SPE) and liquid chromatog. (LC) using peak compression is presented. Protein is precipitated from plasma with acetonitrile-1% aqueous acetic acid (85:15, volume/volume). An internal standard (IS) is added to the samples before they are loaded onto a strong cation exchanger (Isolute PRS) SPE column. PQ and the IS are analyzed by LC on a Zorbax SB-CN column (250 + 4.0 mm) with the mobile phase acetonitrile-phosphate buffer [I = 0.1, pH 2.5 (12:88, volume/volume)] and UV detection at 345 nm. Trichloroacetic acid (TCA) is added to the samples prior to injection into the chromatog. system. PQ elutes in a gradient of TCA, which enables peak compression of PQ and significantly higher peak efficiency as a result. The intraassay precision for plasma is determined to be 5.4% at 3.00μM and 5.8% at 0.050μM. The interassay precision for plasma is 1.3% at 3.00μM and 10.0% at 0.050μM. The lower limit of quantitation and the limit of detection are 0.025 and 0.005 μM, resp. (c) 2003 Preston Publications.
IT **4085-31-8**, Piperaquine
RL: ANT (Analyte); ANST (Analytical study)
(automated solid-phase extraction method for determination of piperaquine in blood plasma by peak compression liquid chromatog.)
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 10 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:549712 HCAPLUS
DOCUMENT NUMBER: 134:26993
TITLE: Prevention and treatment of radiation-induced lung injury by hydroxypiperquin phosphate: A clinical and experimental study
AUTHOR(S): Min, Bihe; Wang, Mei; Xiao, Zuoping; Meng, Peiling; Lan, Li
CORPORATE SOURCE: Department of Hematology, Changhai Hospital, Second Military Medical University, Shanghai, 200433, Peop. Rep. China
SOURCE: Journal of Medical Colleges of PLA (**2000**), 15(1), 76-78
CODEN: JMCPE6; ISSN: 1000-1948

PUBLISHER: Journal of Medical Colleges of PLA, Editorial Board
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We evaluated the hydroxypiperquin phosphate (HPQP) as a modifier of radiation-induced injury in human and rat lungs. Sixty-five patients with lung cancer treated with conventional radiotherapy were divided into 2 groups randomly: Thirty cases were treated with HPQP and the others were in a control group. The changes of X-ray manifestation before, after and during taking drug were compared. An animal model of radiation-induced fibrosis of lungs was also established. Hydroxyproline (HP) content in lung tissue and the pathol. changes in rat lungs were checked with microscope and electron microscope after 4 mo and 6 mo resp. The changes of lung X-ray manifestation in treatment group were much lighter than that in control group. The HP content and the change of pathol. in the lungs of those rats with HPQP treatment were obviously less than that in control group. HPQP plays an important role in prevention and treatment of radiation-induced injury in lungs.
IT **74351-60-3**, Hydroxypiperaquine phosphate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydroxypiperquin phosphate prevention and treatment of radiation-induced lung injury)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 11 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:193186 HCAPLUS
DOCUMENT NUMBER: 131:13355
TITLE: Synthesis of bisquinolines and their in vitro ability to produce methemoglobin in canine hemolyzate
AUTHOR(S): Srivastava, Sandhya; Tewari, Swati; Chauhan, P. M. S.; Puri, S. K.; Bhaduri, A. P.; Pandey, V. C.
CORPORATE SOURCE: Division of Biochemistry, Central Drug Research Institute, Lucknow, 226 001, India
SOURCE: Bioorganic & Medicinal Chemistry Letters (**1999**), 9(5), 653-658
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Synthesis of a number of derivs. of bisquinolines have been reported here. Effect of these compds. on in vitro metHb formation and metHb reductase activity has resulted in the identification of two potential compds. showing negligible metHb toxicity. Structure-activity relations and the use of the compds. to treat malaria are discussed.
IT **95560-84-2P**
RL: ADV (Adverse effect, including toxicity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of bisquinolines and in vitro ability to produce metHb toxicity in canine hemolyzate in relation to structure and antimalarial activity and inhibition of metHb reductase)
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

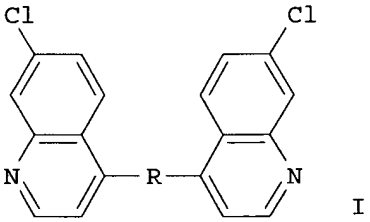
L77 ANSWER 12 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:643422 HCAPLUS
DOCUMENT NUMBER: 130:107178
TITLE: Application and analysis of biochemical indices for

the evaluation of anti-silicosis treatment
AUTHOR(S): Liu, Binci; Qin, Xiaofa
CORPORATE SOURCE: Institute of Occupational Medicine, Chinese Academy of Preventive Medicine, Beijing, 100050, Peop. Rep. China
SOURCE: Weisheng Yanjiu (**1998**), 27(4), 222-224
CODEN: WEYAEM; ISSN: 1000-8020
PUBLISHER: Weisheng Yanjiu Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB 296 Patients with silicosis were received the tetrandrine, polyviylpyridine-N-oxide, hydroxypiperaquinoline phosphate, and aluminum citrate combined therapy, and 144 patients served as control. Serum ceruplasmin (Cp), SOD, and IgG of them were monitored. The SOD level was fluctuating, which was decreased after the 1st and the 6th course, but increased after the 3rd course. The decrease of Cp, SOD, and IgG were consisted with the clin. effectiveness of the treatment. The results suggest that Cp, SOD, and IgG are appropriate biochem. indicators for the evaluation of anti-silicosis drug therapy.

IT **74351-60-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(application and anal. of biochem. indexes for the evaluation of anti-silicosis treatment)

L77 ANSWER 13 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:619254 HCAPLUS
DOCUMENT NUMBER: 129:343400
TITLE: Bisquinolines. 2. Antimalarial N,N-bis(7-chloroquinolin-4-yl)heteroalkanediamines
AUTHOR(S): Vennerstrom, Jonathan L.; Ager, Arba L., Jr.; Dorn, Arnulf; Andersen, Steven L.; Gerena, Lucia; Ridley, Robert G.; Milhous, Wilbur K.
CORPORATE SOURCE: College of Pharmacy, University of Nebraska Medical Center, Omaha, NE, 68198-6025, USA
SOURCE: Journal of Medicinal Chemistry (**1998**), 41(22), 4360-4364
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB N,N-Bis(7-chloroquinolin-4-yl)heteroalkanediamines I [R = HN(CH2)2O(CH2)2NH, HN(CH2)3O(CH2)4O(CH2)3NH, HN(CH2)6NH(CH2)6NH, etc.] were synthesized and screened against Plasmodium falciparum in vitro and Plasmodium berghei in vivo. These bisquinolines had IC50 values from 1 to 100 nM against P. falciparum in vitro. Six of the 11 bisquinolines were significantly more potent against the chloroquine-resistant W2 clone

compared to the chloroquine-sensitive D6 clone. For bisquinolines I, there was no relationship between the length of the bisquinoline heteroalkane bridge and antimalarial activity and no correlation between in vitro and in vivo antimalarial activities. Bisquinolines with alkyl ether and piperazine bridges were substantially more effective than bisquinolines with alkylamine bridges against P. berghei in vivo. Ten of the bisquinolines were potent inhibitors of hematin polymerization with IC50 values falling in the narrow range of 5-20 μM, and there was a correlation between potency of inhibition of hematin polymerization and inhibition of parasite growth. Compared to alkane-bridged bisquinolines (Vennerstrom et al., 1992), none of these heteroalkane-bridged bisquinolines had sufficient antimalarial activity to warrant further investigation of the series.

IT **95560-84-2P 215592-28-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antimalarial activity of bis(chloroquinolinyl)heteroalkanediamines)

IT **837-52-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and antimalarial activity of bis(chloroquinolinyl)heteroalkanediamines)

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 14 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:741260 HCAPLUS
DOCUMENT NUMBER: 128:48119
TITLE: Synthesis of 7-chloro-4-substituted aminoquinolines and their in vitro ability to produce methemoglobin in canine hemolyzate
AUTHOR(S): Srivastava, Sandhya; Tewari, Swati; Srivastave, Sanjay K.; Chauhan, P. M. S.; Bhaduri, A. P.; Puri, S. K.; Pandey, V. C.
CORPORATE SOURCE: Divisions Biochemistry, Medicinal Chem., and Microbiology, Central Drug Research Institute, Lucknow, 226001, India
SOURCE: Bioorganic & Medicinal Chemistry Letters (**1997**), 7(21), 2741-2746
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Synthesis of aminoquinoline derivs. and their in vitro effects on metHb formation and metHb reductase activity are delineated. Some of the screened compds. have shown considerable metHb toxicity. An example compound thus prepared was 2-[(7-chloro-4-quinolinyl)amino]ethanol.

IT **199444-80-9P 199444-81-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of chloroquinolinamine derivs. and their ability to produce metHb in canine hemolyzate)

IT **837-52-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of chloroquinolinamine derivs. and their ability to produce metHb in canine hemolyzate)

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS

L77 ANSWER 15 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:136768 HCAPLUS
DOCUMENT NUMBER: 126:220435
TITLE: Changes of serum type I collagen levels after treated with anti-silicosis drugs
AUTHOR(S): Liu, Bingci; You, Baorong; Wang, Haihua; Miao, Qing; Zou, Changqi
CORPORATE SOURCE: Institute of Occupational Medicine, Chinese Academy of Preventive Medicine, Beijing, 100050, Peop. Rep. China
SOURCE: Weisheng Yanjiu (**1996**), 25(4), 199-201
CODEN: WEYAEM; ISSN: 1000-8020
PUBLISHER: Weisheng Yanjiu Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The effect of tetrandrine (TT), polyvinylpyridine-N-oxide (PVNO), hydroxypiperaquine phosphate and aluminum citrate on the serum levels of type I collagen during silicosis were studied. The rats, expts. showed that TT and PVNO have a strong and stable inhibitive effect on collagen metabolism Hydroxypiperaquine phosphate and aluminum citrate were effective as well, but the collagen levels rose again after the treatments were stopped. Clin. observation revealed that the serum collagen levels were reduced after combined TT and Hydroxypiperaquine phosphate therapy.
IT **74351-60-3**, Hydroxypiperaquine phosphate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(changes in blood serum type I collagen levels in mice after treatment with anti-silicosis drugs)

L77 ANSWER 16 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:63246 HCAPLUS
DOCUMENT NUMBER: 126:122553
TITLE: quantitative determination of piperaquine phosphate by reversed-phase ion-pair high performance liquid chromatography
AUTHOR(S): Chen, Wenliang; Chen, Minjuan; Wu, Hui; Tao, Hongying
CORPORATE SOURCE: Shanghai Zhongxi Pharmaceutical Co., LTD., Shanghai, 200065, Peop. Rep. China
SOURCE: Fenxi Ceshi Yiqi Tongxun (**1995**), 5(2), 93-95
CODEN: FCYTFF; ISSN: 1006-2750
PUBLISHER: Zhongguo Fenxi Ceshi Xiehui
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB An ATTECH ODS (μm) was used as the fixed phase (column, Θ4.6 mm + 150 mm), and the mobile phase consisted of a mixture of methanol-acetonitrile-water-triethylamine-sodium 1-pentanesulfonate (20 mL + 80 mL + 900 mL + 5 mL + 100 mg) which was adjusted to pH 3.0 with phosphoric acid. The flow rate was 1.0 mL/min. The detection wavelength was 240 nm. The RSD(n=10) for the determination of sample containing 99.59% piperaquine phosphate was 0.12% with an average recovery of 100.7%.
IT **85547-56-4**
RL: ANT (Analyte); ANST (Analytical study)
(determination of piperaquine phosphate by reverse phase HPLC)

L77 ANSWER 17 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:345177 HCAPLUS
DOCUMENT NUMBER: 125:25976
TITLE: Therapeutic effect of Xinin, tetrandrine and hydroxypiperaquine phosphate on experimental silicosis

AUTHOR(S): Han, Suli; Zhang, Junying; Du, Qingcheng; Chen, Ningmeng; Cheng, Yuhai
CORPORATE SOURCE: Inst. of Occupational Medicine, Chinese Academy of Preventive Medicine, Beijing, 100050, Peop. Rep. China
SOURCE: Weisheng Yanjiu (**1996**), 25(1), 6-9
CODEN: WEYAEM; ISSN: 1000-8020
PUBLISHER: Weisheng Yanjiu Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB A comparative study of Xinin, tetrandrine and hydroxypiperaquine phosphate on exptl. silicotic rats was carried out. Xinin, tetrandrine and hydroxypiperaquinine phosphate were given to exptl. silicotic rats orally at the dosages of 39 mg kg-1 and 18 mg kg-1, five times a week for 3 mo, resp. These dosages were 1/30 of the median LDs of these three medicines. The dry weight and collagen contents of rat lungs of the treatment groups were much lower than the silicotic control group. No differences in collagen contents in the rat lungs among Xinin, hydroxypiperaquinine phosphate and tetrandrine groups were observed Large formlike cells aggregating in nodules with a slight fibrosis were the main pathol. changes in Xinin and tetrandrine groups. The value of superoxide dismutase and ceruloplasmin contents in the Xinin group were significantly decreased more than those of the silicotic control and other treatment groups.

IT **74351-60-3**, Hydroxypiperaquine phosphate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic effect of Xinin, tetrandrine and hydroxypiperaquine phosphate on exptl. silicosis)

L77 ANSWER 18 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:932779 HCAPLUS
DOCUMENT NUMBER: 124:21255
TITLE: Reversing effect of tripiperaquine on human multidrug-resistant leukemic cell line K562/A02
AUTHOR(S): Yang, Renchi; Yang, Chunzheng; Hao, Yushu; Qi, Jing
CORPORATE SOURCE: Inst. Hematology, CAMS, Tianjin, 300020, Peop. Rep. China
SOURCE: Zhonghua Zhongliu Zazhi (**1995**), 17(5), 340-2
CODEN: CCLCDY; ISSN: 0253-3766
PUBLISHER: Zhongguo Yixue Kexueyuan Zhongliu Yanjiuso
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB K562/A02 is a cell line with multidrug resistance (MDR) established by long-term induction with adriamycin. The reversal of MDR in K562/A02 cells by tripiperaquine is reported. The cytotoxicity and intracellular concentration of daunorubicin (DNR) in K562/A02 cells were measured. The sensitivity of K562/A02 to DNR was greatly enhanced by tripiperaquine at 10 μg/mL, with an 11-fold increase in cytotoxic activity. The intracellular concentration of DNR in K562/A02 cells was increased after coincubation with 20 μM tripiperaquine for 3 h. Tripiperaquine might be used in clin. trials to reverse MDR.

IT **53658-96-1**, Tripiperaquine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(reversal of resistance of human leukemia cells to daunorubicin by tripiperaquine)

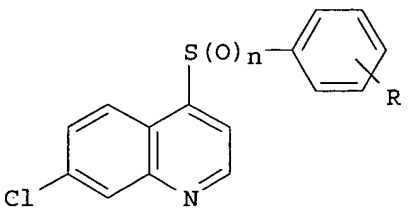
L77 ANSWER 19 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:788263 HCAPLUS

DOCUMENT NUMBER: 123:246391
TITLE: Antiarrhythmic effects of piperaquine phosphate in experimental arrhythmias
AUTHOR(S): Wang, Weizhi; Liang, Rixin; Xiao, Zhijie; Zhao, Yanjie
CORPORATE SOURCE: Dep. Pharmacol., Jinzhou Medical Coll., Jinzhou, 121004, Peop. Rep. China
SOURCE: Zhongguo Yaolixue Tongbao (**1993**), 9(4), 284-6
CODEN: ZYTOE8; ISSN: 1001-1978
PUBLISHER: Anhui Yike Daxue Linchuan Yaoli Yanjiuso
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

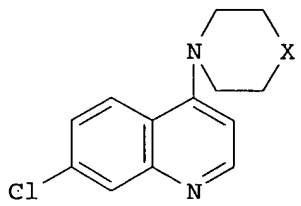
AB Piperaquine phosphate (PQP) 9 mg·kg-1, i.v., markedly reduced the mortality of mice induced by CaCl2 130 mg·kg-1, i.v. PQP 18 mg·kg-1, i.p., prevented mice from chloroform-induced ventricular fibrillation (VF). In the anesthetized rats, PQP 6.3 mg·kg-1, i.v., significantly elevated the dose of aconitine 2 mg·min-1, i.v., required to induced ventricular extrasystole (VE), ventricular tachycardia (VT) and (VF)·POP 5.4 mg·kg-1 dramatically increased the dose of ouabain 10 μg·min-1, i.v., required to induced VE, VT and VF in the anesthetized guinea pigs. PQP 3.3 mg·kg-1, i.v. greatly shortened the duration of arrhythmia elicited by epinephrine 50 μg·kg-1, i.v., in unanesthetized rabbits. The results suggested that PQP exerted antiarrhythmic actions in animals. The i.v. LD50 of PQP in mice was 93.33 mg·kg-1.

IT **85547-56-4**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiarrhythmic effects of piperaquine phosphate in exptl. arrhythmias)

L77 ANSWER 20 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:333441 HCAPLUS
DOCUMENT NUMBER: 122:160450
TITLE: Synthesis of 4-arylsulfonyl/piperazinyl-7-chloroquinolines and related compounds as potential antimalarial agents
AUTHOR(S): Tripathi, R. C.; Saxena, M.; Chandra, S.; Saxena, Anil K.
CORPORATE SOURCE: Central Drug Research Institute, Lucknow, 226 001, India
SOURCE: Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (**1995**), 34B(2), 164-6
CODEN: IJSBDB; ISSN: 0376-4699
PUBLISHER: Publications & Information Directorate, CSIR
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 122:160450
GI



I

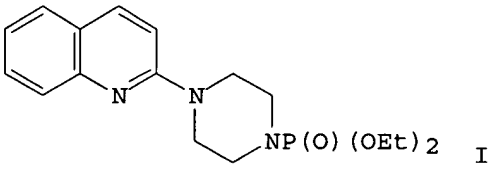


II

AB The title compds. I (n = 2; R = 3-Cl, 4-Me, etc.) and II (X = NH, NCOPh, CH2, etc.) have been synthesized by condensation of the key intermediate 4,7-dichloroquinoline with substituted thiophenols and secondary cyclic amines to give the corresponding sulfides I (n = 0) and amines, followed by oxidation of the sulfides. The sulfones I (n = 2) and the amines II have been evaluated for their blood schizontocidal activity and reversal of chloroquine resistance activity. None of these compds. showed any significant activity.

IT **837-52-5P 161467-82-9P 161467-83-0P**
161467-84-1P 161467-85-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of (arylsulfonyl)- or piperazinylchloroquinolines and related compds. as potential antimalarial agents)

L77 ANSWER 21 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1993:495665 HCAPLUS
DOCUMENT NUMBER: 119:95665
TITLE: Piperazinylquinoline amidophosphates: synthesis and study of their action on blocked reverse serotonin uptake
AUTHOR(S): Sidorin, D. N.; Kozyukov, A. V.; Zakharova, V. A.; Porodenko, N. V.; Kryukov, L. N.
CORPORATE SOURCE: VNTSentr Mol. Diagn. Lechen., Moscow, Russia
SOURCE: Khimiko-Farmatsevticheskii Zhurnal (**1992**), 26(9-10), 82-3
CODEN: KHFZAN; ISSN: 0023-1134
DOCUMENT TYPE: Journal
LANGUAGE: Russian
GI



I

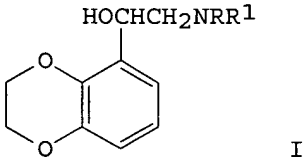
AB Todd-Atherton phosphorylation of (1-piperazinyl)quinoline derivs. with di-Et phosphite afforded the corresponding quinoline piperazinylamidophosphate derivs. in 30-40% yield. Antidepressant activity (inhibition of reverse uptake of serotonin) of the amidophosphate derivs. exceeded that of the starting materials, with title compound I most active (IC50 2.0 nM).

IT **837-52-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antidepressant activity of, and of its phosphorylated derivative)

IT **149144-34-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and antidepressant activity of)

L77 ANSWER 22 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1993:495477 HCAPLUS
DOCUMENT NUMBER: 119:95477
TITLE: Synthesis of piperazinylquinolines and study of their effects on the activity of protein kinase C
AUTHOR(S): Sidorin, D. N.; Tubasheva, I. A.; Alisova, V. I.; Severin, S. Ye.; Kryukov, L. N.
CORPORATE SOURCE: Vses. Nauchn. Tsentr. Mol. Diagn. Lechen., Moscow, Russia
SOURCE: Khimiko-Farmatsevticheskii Zhurnal (**1992**), 26(9-10), 37-9
CODEN: KHFZAN; ISSN: 0023-1134
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB Of the piperazinylquinolines prepared, 4-(1-piperazinyl)-7-chloroquinoline displayed the highest activity for inhibition of protein kinase C (240 mM).
IT **837-52-5P 149225-73-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and inhibiting activity of, for protein kinase C)

L77 ANSWER 23 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1993:233972 HCAPLUS
DOCUMENT NUMBER: 118:233972
TITLE: 1-(2,3-Dihydro-1,4-benzodioxin-5-yl)-2-aminoethanols. Synthesis and antihypertensive properties
AUTHOR(S): Perdicakis, C.; Coudert, G.; Lalloz, L.; Lamar, J. C.; Guillaumet, G.
CORPORATE SOURCE: Fac. Pharm., Univ. Nancy I., Nancy, F-54000, Fr.
SOURCE: Scientia Pharmaceutica (**1992**), 60(1/2), 27-40
CODEN: SCPHA4; ISSN: 0036-8709
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB The title compds. I (NRR1 = NHCHMe2, substituted piperidino, piperazino, tetrahydroisoquinolinyl) were prepared from 2,3-(HO)2C6H3CO2H or 2,3-(HO)2C6H3CHO via the halo alcs., followed by nucleophilic substitution with selected amines in DMF or HMPA. I [R = 4-(2-methoxyphenyl)piperazino, II] at 25 mg/kg orally in the renal hypertensive dog, decreased blood pressure by ≤ 56% for >5 h. II is also a potent α-adrenoceptor antagonist.
IT **147587-90-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and antihypertensive and α- and β-adrenergic antagonistic activity of)

L77 ANSWER 24 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1992:39012 HCAPLUS
DOCUMENT NUMBER: 116:39012
TITLE: Determination of low-content glycogen in the kidney cortex of diabetic rats
AUTHOR(S): Oi, Kazuteru; Ihara, Hiroshi; Shimoda, Yuko; Toyoda, Masateru
CORPORATE SOURCE: Sch. Med., Toho Univ., Tokyo, 153, Japan
SOURCE: Seibutsu Shiryo Bunseki (**1990**), 13(1), 38-40
CODEN: SSBUEL; ISSN: 0913-3763
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Acid hydrolysis and enzymic glucose determination were used to determine tissue glycogen. Good results were obtained, and the method was useful for tissue glycogen determination even in the kidney with a low-glycogen content.
IT **900-57-2**
RL: BIOL (Biological study)
(of kidney, acid hydrolysis and enzymic glucose determination in study of)

L77 ANSWER 25 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:549554 HCAPLUS
DOCUMENT NUMBER: 115:149554
TITLE: Recent studies on antimalarial efficacy of piperaquine and hydroxypiperaquine
AUTHOR(S): Lin, Chen
CORPORATE SOURCE: Lab. Antimalar. Drug Res., 2nd Mil. Med. Univ., Shanghai, 200433, Peop. Rep. China
SOURCE: Chinese Medical Journal (Beijing, China, English Edition) (**1991**), 104(2), 161-3
CODEN: CMJODS; ISSN: 0366-6999
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 10 refs.
IT **4085-31-8**, Piperaquine **74351-59-0**, Hydroxypiperaquine
RL: BIOL (Biological study)
(antimalarial efficacy of)

L77 ANSWER 26 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:466407 HCAPLUS
DOCUMENT NUMBER: 115:66407
TITLE: Pathological observation of experimental asbestosis treated by hydroxypiperquin phosphate in dogs
AUTHOR(S): Li, Hongyang; Wu, Zhongshun; Zeng, Ximing; Liu, Shaoquan; Zheng, Zhiren; Zeng, Lin; Duanmu, Binru; Ke, Fuxin; Yang, Huiru; Qing, Yuxiao
CORPORATE SOURCE: Dep. Pathol., West China Univ. Med. Sci., Chengdu, Peop. Rep. China
SOURCE: Huaxi Yike Daxue Xuebao (**1991**), 22(2), 181-4
CODEN: HYDXET; ISSN: 0257-7712
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The paper presents exptl. asbestosis treated with hydroxypiperquin phosphate (HPQP) in dogs. Results showed that the total cell number of bronchoalveolar lavage fluid, the viability of alveolar macrophages and the enzyme activities of lactate dehydrogenase, acid phosphatase and β-glucuronidase of alveolar macrophages in treated dogs were higher than those in exposed dogs; asbestos fibers contents in the lungs and the mean scores of lung lesions in the treated dogs were markedly less than those in the exposed dogs. These findings support that HPQP may play a

role in protecting alveolar macrophages from damage and inhibiting the progression of lung fibrosis; the clin. application of HPQP is evidenced by this study.

IT **74351-60-3**, Hydroxypiperaquine phosphate
RL: BIOL (Biological study)
(exptl. asbestosis treatment with, lung pathol. in)

L77 ANSWER 27 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:584475 HCAPLUS
DOCUMENT NUMBER: 113:184475
TITLE: Effect of hydroxypiperaquine phosphate on the slow response action potential in guinea-pig papillary muscles and rabbit sinus node cells
AUTHOR(S): Li, Husong; Zhao, Gengsheng; Li, Xiaoguang
CORPORATE SOURCE: Inst. Clin. Pharmacol., Xian Med. Univ., Xian, 710061, Peop. Rep. China
SOURCE: Zhongguo Yaolixue Yu Dulixue Zazhi (**1990**), 4(3), 176-9
CODEN: ZYYZEW; ISSN: 1000-3002
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB Effects of hydroxypiperaquine phosphate (HPQP) on slow response action potentials were investigated in the papillary muscles and sinus node cells. In the K+-depolarized papillary muscles, HPQP at 100 μM reduced amplitude of action potential (APA) from 73 to 62 mV and maximal upstroke velocity (.ovrhdot.Vmax) from 4.2 to 2.8 V/s, but it did not affect the anion potential duration at 90% repolarization (APD90). The inhibition of HPQP on .ovrhdot.Vmax showed a dose- and frequency-dependent way. Ventricular autorhythmicity induced by Ba2+ was suppressed and the cycle of spontaneous beat was prolonged from 640 to 694 ms at 30 μM. Effect of HPQP at 100 μM on the sinus node dominant pacemaker cells showed that APA and .ovrhdot.Vmax were decreased from 53 of control to 48 mV and from 1.84 to 1.26 V/s, resp. APD50, APD100, and spontaneous cycle length were lengthened from 83 of control to 181 ms, from 186 to 193 ms and from 498 to 802 ms, resp. The slope of diastolic depolarization was smoothed down. These results suggest that HPQP may block calcium channels, which would contribute the antiarrhythmic action.

IT **74351-60-3**
RL: BIOL (Biological study)
(heart sinus node and ventricle elec. activity response to, antiarrhythmic action in relation to)

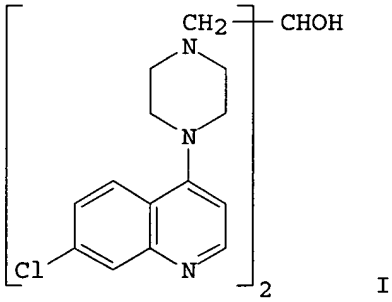
L77 ANSWER 28 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:584474 HCAPLUS
DOCUMENT NUMBER: 113:184474
TITLE: Effect of hydroxypiperaquine phosphate on action potential and contractile force of guinea pig heart muscles
AUTHOR(S): Li, Husong; Zhao, Gengsheng
CORPORATE SOURCE: Inst. Clin. Pharmacol., Xian Med. Univ., Xian, 710061, Peop. Rep. China
SOURCE: Zhongguo Yaolixue Yu Dulixue Zazhi (**1990**), 4(3), 173-5
CODEN: ZYYZEW; ISSN: 1000-3002
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB The effects of hydroxypiperaquine phosphate (HPQP) on the elec. and mech. activities of the isolated right ventricular papillary muscles of guinea pigs were studied by conventional glass microelectrodes. HPQP at 30 μM inhibited contractile force from 100% of control to 70.6% and decreased

maximal upstroke velocity from 270 to 238 V/s. At the same concentration, HPQP prolonged action potential duration at 20 and 90% repolarization (APD20, APD90) from 116 to 125 ms and from 230 to 238 ms, resp. The effective refractory period was distinctly increased from 214 to 235 ms. HPQP at 100 μM reduced the amplitude of action potential from 118 to 114 mV. All these results showed a concentration-dependent manner above 10 μM. HPQP at 30 μM could antagonize the effect of acetylcholine (10 μM) on shortening APD in atria. Moreover, HPQP at 100 μM diminished or eliminated the oscillatory potential induced by ouabain (0.4-1.5 μM). These results indicate that HPQP may unspecifically inhibit the transmembrane currents of Na+, Ca2+, and K+.

IT **74351-60-3**
RL: BIOL (Biological study)
(heart elec. activity and contractile force response to)

L77 ANSWER 29 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:434249 HCAPLUS
DOCUMENT NUMBER: 113:34249
TITLE: New antimalarial and antisilicosis drug hydroxypiperaquine
AUTHOR(S): Xu, Deyu; Shen, Nianci; Yin, Muquan; Yin, Xiangsheng; Li, Yutang
CORPORATE SOURCE: 2nd Mil. Med. Coll., Shanghai, 200433, Peop. Rep. China
SOURCE: Zhongguo Yiyao Gongye Zazhi (**1989**), 20(11), 488-93
CODEN: ZYGZEA; ISSN: 1001-8255
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
GI



I

AB A review, with 13 refs., of the chemical, pharmacol., and toxicity of a new antimalarial and antisilicosis drug, hydroxypiperaquine (I).

IT **74351-59-0**, Hydroxypiperaquine
RL: BIOL (Biological study)
(antimalarial and antisilicosis pharmacol. of, in humans and laboratory animals)

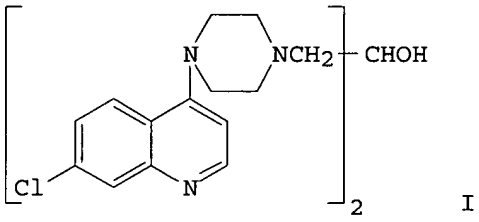
L77 ANSWER 30 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1989:451902 HCAPLUS
DOCUMENT NUMBER: 111:51902
TITLE: Reproductive toxicity and genotoxicity of piperaquine phosphate
AUTHOR(S): Wang, Minming; Yao, Yulong; Yang, Jinming; Zhao, Huiqiu

CORPORATE SOURCE: Shanghai Inst. Pharm. Ind., Shanghai, Peop. Rep. China
SOURCE: Zhongguo Yiyao Gongye Zazhi (**1989**), 20(3), 120-4
CODEN: ZYGZEA; ISSN: 1001-8255
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB Pregnant rats and rabbits were given piperaquine phosphate at the doses of 12, 40, or 120 mg/kg/d. No teratogenic effects were observed However, the embryotoxicity was found for the dose of 120 mg/kg/d. Examination of chromosomal aberration of spermatogonial cell and PCE micronucleus test showed neg. results at the cited doses PO in ICR mice.

IT **85547-56-4**
RL: BIOL (Biological study)
(reproductive toxicity and genotoxicity of)

L77 ANSWER 31 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:583092 HCAPLUS
DOCUMENT NUMBER: 109:183092
TITLE: Studies on the new antimalarial drug hydroxypiperaquine and its phosphate
AUTHOR(S): Xu, Deyu; Shen, Nianci; Li, Yutang; Yin, Muquan; Wang, Xiaopeng; Li, Jun; Gong, Jianzhang
CORPORATE SOURCE: Lab. Antimalarial Drug Res., 2nd Mil. Med. Coll., Shanghai, Peop. Rep. China
SOURCE: Journal of Medical Colleges of PLA (**1988**), 3(1), 5-12
CODEN: JMCPE6; ISSN: 1000-9094
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

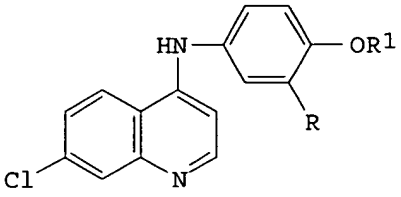
AB The preparation of hydropiperaquine (I) and its phosphate salt and studies on its antimalarial activity and toxicity are described.

IT **74351-59-0P 74351-60-3P**
RL: ADV (Adverse effect, including toxicity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antimalarial activity and toxicity of)

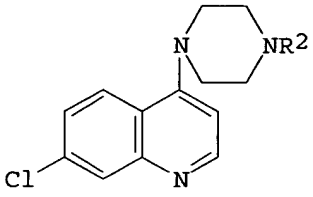
L77 ANSWER 32 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:186530 HCAPLUS
DOCUMENT NUMBER: 108:186530
TITLE: Antiparasitic agents. Part VI. Synthesis of 7-chloro-4-(4-substituted-phenylamino)- and 7-chloro-4-(4-substituted-piperazin-1-yl)quinolines as potential antiparasitic agents
AUTHOR(S): Agrawal, Vijai K.; Sharma, Satyavan
CORPORATE SOURCE: Med. Chem. Div., Cent. Drug Res. Inst., Lucknow, 226 001, India

SOURCE: Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (1987), 26B(6), 550-5
CODEN: IJSBDB; ISSN: 0376-4699
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 108:186530

GI



I



II

AB Chloro(hydroxyphenylamino)quinolines I (R = H, CO2H, NO2, NH2, substituted carbamoyl, R1 = H, C6H4OMe-2, C6H4Me-3, C6H4Me-4), chloro(4-piperazinyl)quinolines II (R2 = H, substituted carbamoyl, substituted carbamoylmethyl), and other similar compds. were prepared and tested for their antimalarial, antifilarial and antimicrobial activities but none of them shows any noteworthy activity.

IT **837-52-5P 104692-85-5P 114259-98-2P**
114259-99-3P 114260-00-3P 114260-01-4P
114260-02-5P 114260-03-6P 114260-04-7P
114260-05-8P 114260-06-9P 114260-07-0P
114260-08-1P 114282-73-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and antimalarial, antifilarial, and antimicrobial activities of)

L77 ANSWER 33 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:87628 HCAPLUS
DOCUMENT NUMBER: 108:87628
TITLE: Effects of artesunate, pyronaridine, and hydroxypiperaquine on chloroquine-sensitive and chloroquine-resistant isolates of Plasmodium falciparum in vitro
AUTHOR(S): Li, Jun; Huang, Wenjin
CORPORATE SOURCE: Dep. Parasitol., 2nd Mil. Med. Coll., Shanghai, 200433, Peop. Rep. China
SOURCE: Zhongguo Yaoli Xuebao (1988), 9(1), 83-6
CODEN: CYLPDN; ISSN: 0253-9756
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB Little difference was found in the sensitivity of chloroquine-sensitive and -resistant isolates of P. falciparum to artesunate, pyronaridine, and hydroxypiperaquine, as determined by microtechnique in vitro. Apparently, no cross resistance occurs between chloroquine and these 3 antimalarials.

IT **74351-59-0**
RL: BIOL (Biological study)
(chloroquine-sensitive and -resistant Plasmodium falciparum response to)

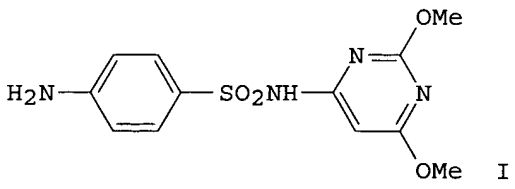
L77 ANSWER 34 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1987:549825 HCAPLUS

DOCUMENT NUMBER: 107:149825
TITLE: Determinations of activity of the globinase from Plasmodium berghei by radiometry with mouse [3H]globin as substrate
AUTHOR(S): Zhu, Meiying; Gu, Haoming
CORPORATE SOURCE: Shanghai Inst. Mater. Med., Acad. Sin., Shanghai, 200031, Peop. Rep. China
SOURCE: Zhongguo Yaoli Xuebao (**1987**), 8(4), 351-5
CODEN: CYLPDN; ISSN: 0253-9756
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

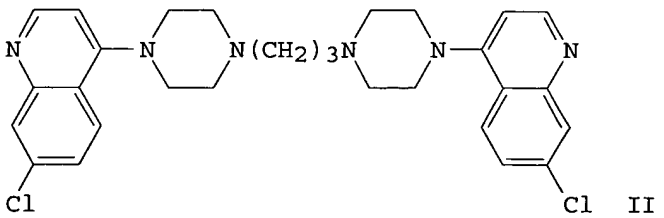
AB For the determination of globinase, an induction of reticulocytes in mouse blood of 60% was achieved by i.p. injection of phenylhydrazine hydrochloride 15 mg/kg twice a day for 8 days. [4,5-3H]leucine was used as a precursor to label the Hb being synthesized in a cell-system in vitro consisting of the reticulocytes. Then, [3H]globin was prepared from the [3H]Hb. Assays of the activity of the globinase from P. berghei were performed by using [3H]globin as a substrate. There was no elevation in activity of the globinase from the strain of P. berghei resistant to hydroxypiperaquine compared to that from the ANKA strain of P. berghei sensitive to antimalarials. The affecting factors were also investigated on removal of white cells from malaria-infected blood and on detns. of activity of the globinase in the lysate or extract from P. berghei.

IT **74351-59-0**
RL: BIOL (Biological study)
(Plasmodium berghei resistance to, globinase activity in relation to)

L77 ANSWER 35 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1986:597259 HCAPLUS
DOCUMENT NUMBER: 105:197259
TITLE: Derivative spectrophotometric determination of sulfadimoxine and piperaquine in tablets
AUTHOR(S): Shen, Kewen; Han, Yongping
CORPORATE SOURCE: Inst. Drug Cent., PLA, Beijing, Peop. Rep. China
SOURCE: Yiyao Gongye (**1986**), 17(6), 270-4
CODEN: YIGODN; ISSN: 0255-7223
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
GI



I



II

AB Sulfadimoxine (I) [122-11-2] and piperaquine (II) [**4085-31-8**] were determined in their sep. compound tablets by derivative spectrophotometry. A 2nd derivative spectrophotometric method was used for I determination which eliminated interferences from excipients. II could be determined either by 1st or 2nd derivative methods. The recovery was close to 100%.

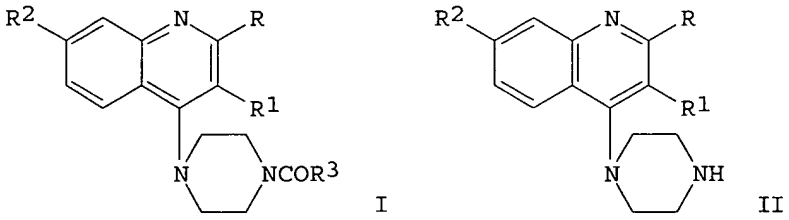
IT **4085-31-8**
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in tablets by derivative spectrophotometry)

L77 ANSWER 36 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1986:583455 HCAPLUS
DOCUMENT NUMBER: 105:183455
TITLE: Evaluation of phototoxic effects of chlorquine and eleven other antimalarials in mice
AUTHOR(S): Yuan, Bojun; Li, Baochun; Shen, Nianci
CORPORATE SOURCE: Lab. Antimalar. Drug Res., 2nd Mil. Med. Coll., Shanghai, Peop. Rep. China
SOURCE: Zhongguo Yaoli Xuebao (**1986**), 7(5), 468-70
CODEN: CYLPDN; ISSN: 0253-9756
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB No phototoxicity was observed within 7 days in mice treated with an oral 0.25 LD50 of chloroquine [54-05-7] or 11 other antimalarials and irradiated under black light at 22° for 24 h; i.v. injection of chloroquine, piperaquine [**4085-31-8**], hydroxypiperaquine [**74351-60-3**], or quinine [130-95-0] at 0.25-0.5 LD50 did not cause phototoxicity. I.p. injection of one of these 4 drugs or mefloquine [53230-10-7] at 0.125 LD50/day for 7 days into mice (irradiated for 8 h/day) also did not produce phototoxicity.

IT **4085-31-8 74351-60-3**
RL: BIOL (Biological study)
(phototoxicity from)

L77 ANSWER 37 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1986:564484 HCAPLUS
DOCUMENT NUMBER: 105:164484
TITLE: Studies on aminoquinolines. Chemical, antiparasitic, antimicrobial and antifungal studies of 4-(4-mono-, di- and trichloroacetyl-1-piperazinyl)quinolines
AUTHOR(S): Gauthier, B.; Renault, J.; Gobert, J. G.; Leluan, G.; Bournazel, C.; Duault, M.
CORPORATE SOURCE: Dep. Chim. Org., Univ. Rene-Descartes, Paris, F 75270, Fr.
SOURCE: Annales Pharmaceutiques Francaises (**1986**), 44(1), 55-64
CODEN: APFRAD; ISSN: 0003-4509
DOCUMENT TYPE: Journal
LANGUAGE: French
GI



I II

AB Piperazinylquinolines (I, R = H, Me; R1 = H, Cl, CF3, NO2; R2 = Cl, CF3, OMe; R3 = H, CH2ClCHCl2, CCl3 and II, R = H, Me; R1 = H, NO2; R2 = H, Cl, CF3, OMe) were prepared and their pharmacol. was studied. I were prepared either by the reaction of 1-nitrosopiperazines with chloroquinolines, hydrogenolysis of the chloro(nitrosopiperazinyl)quinolines, and chloroacetylation of the resultant II or by reaction of piperazine [**104667-94-9**] with chloroquinolines followed by chloroacetylation. The parasiticidal, antibacterial and antifungal activities of I and II were studied in vitro. The amebicidal activity of the compds. was studied both in vitro and in vivo. The chloroacetyl derivs. showed weak bactericidal activity. The structure-activity relations of the compds. are discussed.

IT **32863-63-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenolysis of)

IT **837-52-5P 31502-87-1P 104667-94-9P 104667-95-0P 104692-85-5P**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(preparation and pharmacol. of)

IT **104668-07-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

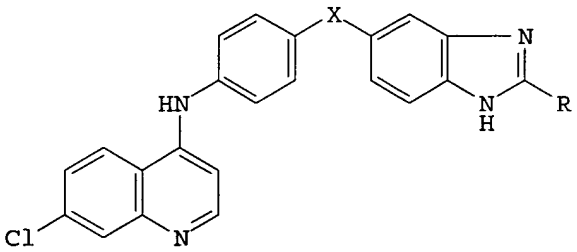
L77 ANSWER 38 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1986:494367 HCAPLUS
DOCUMENT NUMBER: 105:94367
TITLE: Effects of piperaquine on fine structure of erythrocytic stages of Plasmodium berghei ANKA strain
AUTHOR(S): Chen, Lin; Qian, Yongle; Li, Zelin; Zhang, Kuihan; Dai, Baoqiang; Liu, Zefu; Wang, Jinlin
CORPORATE SOURCE: Lab. Antimalarial Drug Res., 2nd Mil. Med. Coll., Shanghai, 200433, Peop. Rep. China
SOURCE: Zhongguo Yaoli Xuebao (**1986**), 7(4), 351-3
CODEN: CYLPDN; ISSN: 0253-9756
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB Piperaquine, 1,3-bis(4-(7-chloroquinolyl-4)-piperazinyl-1)-propane, is superior to chloroquine in suppressing malaria parasites, even chloroquine-resistant I-III P. falciparum, with a relatively long preventive activity. The effects of piperaquine (ED50 6.4 mg base/kg) on the fine structure of the erythrocytic stages of P. berghei ANKA strain indicated that piperaquine exerted its effects mainly on the ameboid trophozoites. No marked effects on the ring forms, immature or mature schizonts, or male and female gametocytes were observed A proportion of the

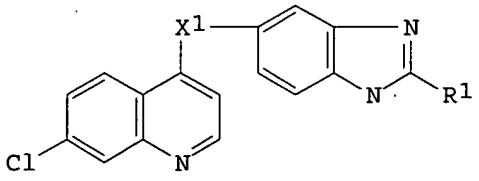
trophozoites showed progressive morphol. changes such as swelling of the food vacuole membrane 1 h after medication. At 4 h after exposure to piperaquine, swelling of mitochondria, proliferation of the multilamellate membrane body (MB), and enlarged digestive vacuoles containing round or oval pigment grains in clusters were observed In some trophozoites, the pigment grains exhibited a very dense appearance. The intermembranous space between the outer and inner nuclear membranes was swollen. Occasionally, aggregations of chromatin material were prominent within the nucleus 12 h after medication. Autophagocytosis became so marked that most of the parasites were disintegrated and only some membranous residues remained 12-24 h after medication. These results suggest that piperaquine first interferes with the physiol. function of the food vacuole membrane of the trophozoites. For comparison, the effects of chloroquine on the fine structure of the parasites were also investigated.

IT **4085-31-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(Plasmodium berghei response to)

L77 ANSWER 39 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1986:442720 HCAPLUS
DOCUMENT NUMBER: 105:42720
TITLE: Syntheses of 2,5(6)-disubstituted benzimidazoles and 1,4-disubstituted piperazines as potential antiparasitic agents
AUTHOR(S): Abuzar, Syed; Dubey, Rashmi; Sharma, Satyavan
CORPORATE SOURCE: Med. Chem. Div., Cent. Drug Res. Inst., Lucknow, 226 001, India
SOURCE: Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (**1985**), 24B(8), 848-52
CODEN: IJSBDB; ISSN: 0376-4699
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 105:42720
GI



I



II

AB Quinoline-containing benzimidazoles I (X = O, S; R = H, Me, NHCO2Et, NHCO2Me)

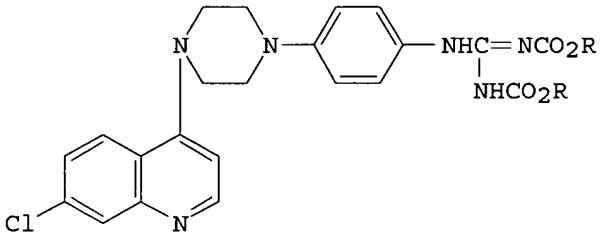
and II (X1 = NH, 1,4-piperazinediyl; R1 = H, NHCO2Me, NHCO2Et) were prepared from 4,7-dichloroquinoline. I and II were tested for antimalarial activity against Plasmodium berghei in mice, antihookworm activity against Ancylostoma ceylanicum in hamsters, and anticestode activity against Hymenolepis nana in rats and mice.

IT **103248-81-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclocondensation reactions of, with (alkoxycarbonyl)isothioureas)

IT **103248-80-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reduction of)

IT **103248-82-4P 103248-83-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

L77 ANSWER 40 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1986:435178 HCAPLUS
DOCUMENT NUMBER: 105:35178
TITLE: Synthesis of some new 7-chloro-4-substituted quinolines as potential antiparasitic agents. (1)
AUTHOR(S): Abuzar, Syed; Dubey, Rashmi; Sharma, Satyavan
CORPORATE SOURCE: Med. Chem. Div., Cent. Drug Res. Inst., Lucknow, 226001, India
SOURCE: European Journal of Medicinal Chemistry (**1986**), 21(1), 5-8
CODEN: EJMCA5; ISSN: 0223-5234
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 105:35178
GI



I

AB 7-Chloro-4-substituted quinolines were prepared and tested for activity against Plasmodium berghei infection in mice, Ancylostoma ceylanicum (Hookworm) infestation in hamsters, Hymenolepis nana (cestode) infection in rats, and Litomosoides carinii (filaria) infection in cotton rats. Except for I; R = Me [**103085-91-2**] and I; R = Et [**103086-26-6**], which were active against L. carinii infection, all other compds. were inactive against the parasites studied.

IT **103085-91-2P 103086-08-4P 103086-09-5P 103086-10-8P 103086-11-9P 103086-12-0P 103086-26-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and antiparasitic activity of)

L77 ANSWER 41 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1986:400231 HCAPLUS
DOCUMENT NUMBER: 105:231
TITLE: Evaluation of phototoxicity of five antimalarial agents and praziquantel in mice
AUTHOR(S): Shao, Baoruo; Zhan, Chongqin; Ha, Shuhua
CORPORATE SOURCE: Inst. Parasitic Dis., China Natl. Cent. Prevent. Med., Shanghai, Peop. Rep. China
SOURCE: Zhongguo Yaoli Xuebao (**1986**), 7(3), 273-5
CODEN: CYLPDN; ISSN: 0253-9756
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB Slightly phototoxic reactions (swelling and erythema) were seen in mice exposed to UV radiation for 24 h after intragastric gavage of chloroquine [54-05-7] (300-600 mg/kg), piperaquine [**4085-31-8**] (549-1098 mg/kg) nitroquine [29972-31-4] (26.7-53.5 mg/kg), and praziquantel [55268-74-1] (2180-2500 mg/kg). No phototoxicity was noted in mice given pyronaridine [74847-35-1] (800 mg/kg) and quinacrine [83-89-6] (1500 mg/kg).
IT **4085-31-8**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (phototoxicity of)

L77 ANSWER 42 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1986:148706 HCAPLUS
DOCUMENT NUMBER: 104:148706
TITLE: Syntheses of 4-(aryl/arylcarbonyl)amino- and 4-arylthio/arylsulfonyl-7-chloroquinolines as potential antiparasitic agents
AUTHOR(S): Dubey, Rashmi; Abuzar, Syed; Sharma, Satyavan
CORPORATE SOURCE: Med. Chem. Div., Cent. Drug Res. Inst., Lucknow, 226 001, India
SOURCE: Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (**1985**), 24B(4), 408-13
CODEN: IJSBDB; ISSN: 0376-4699
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 104:148706
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The syntheses of (arylcarbonylamino)chloroquinolines e.g. I [R = CO2R1, C(:NCO2R1)NHCO2R1; R1 = Me, Et, Me2CHCH2) and II (R1 = Me, Et), (arylamino)chloroquinolines e.g. III (X = 1,2-C6H4, 1,4-C6H4) and IV (R2 = 5-benzofuranyl, 2-methyl-6-benzothiazolyl), 1-(7-chloroquinolin-4-yl)-4-(2-pyridyl)piperazine and 7-chloroquinolines e.g. V [R3 = H, NO2, PhS, NH2, NHC(:NCO2R1)NHCO2R1; n = 0, 2] have been carried out starting from 4,7-dichloroquinoline. The compds. have been tested for their blood schizontodicidal activity against Plasmodium berghei in mice and for anthelmintic activity against Ancylostoma ceylanicum in hamsters and Litomosoides carinii in cotton rats. However, none of the compds. tested shows any significant activity.
IT **100672-05-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of)

L77 ANSWER 43 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1986:3319 HCAPLUS
DOCUMENT NUMBER: 104:3319
TITLE: Plasmodium falciparum in Madagascar: in vivo and in vitro sensitivity to seven drugs
AUTHOR(S): Deloron, P.; Le Bras, J.; Ramanamirija, J. A.; Coulanges, P.
CORPORATE SOURCE: Inst. Med. Epidemiol. Trop., Hop. Claude Bernard, Paris, 75944/19, Fr.
SOURCE: Annals of Tropical Medicine & Parasitology (**1985**), 79(4), 357-65
CODEN: ATMPA2; ISSN: 0003-4983
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The sensitivity level of P. falciparum isolates to chloroquine and the activity of 6 other antimalarials were studied in the different climatic zones of Madagascar in 1983. In vivo tests were done with 10 and 25 mg kg-1 of chloroquine and amodiaquine. Early recrudescence or RII resistance was observed after treatment with 10 mg kg-1 of these drugs in 34% of the cases for chloroquine and 6·5% for amodiaquine, and after the 25 mg kg-1 dose, in 7% and 0% of the cases resp. In vitro sensitivity of 84 P. falciparum isolates to 7 drugs were studied with a semi-microtest. For chloroquine, 9% of the isolates had an IC50 >250 nM, indicating resistance. In vitro activity of piperaquine was high for all except 2 isolates. In vitro activity of amodiaquine, dichlorquinazine, quinine, mefloquine, and halofantrine was good against all isolates (maximum IC50 was 76, 92, 560, ≤20, and ≤12 nM, resp.). The correlation between the WHO standard field test and the in vitro semi-microtest was good. The resistance of P. falciparum to chloroquine was observed in the 6 survey areas, but the other tested drugs showed good activity. Since no cross-resistance to 4-aminoquinolines seems to exist in Madagascar, amodiaquine should be studied as an alternative to choroquine in the prevention and treatment of falciparum malaria.
IT **99461-88-8**
RL: BIOL (Biological study)
(Plasmodium falciparum sensitivity to, in vitro and in vivo)

L77 ANSWER 44 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1985:610932 HCAPLUS
DOCUMENT NUMBER: 103:210932
TITLE: Development of piperaquine-resistant line of Plasmodium berghei K173 strain
AUTHOR(S): Li, Gaode
CORPORATE SOURCE: Lab. Antimalarial Drug Res., 2nd Mil. Med. Coll., Shanghai, Peop. Rep. China
SOURCE: Yaoxue Xuebao (**1985**), 20(6), 412-17
CODEN: YHHPAL; ISSN: 0513-4870
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB A piperaquine-resistant (PR) cell line of P. berghei was developed by repeated passages in the presence of gradually increasing concns. of the drug. The starting concentration of piperaquine was 7 mg/kg (ED50) and was increased by 3.5 mg/kg every 3 passages. At passage number 7, 13, and 20, the resistance of the cells were increased 3.5-, 75-, and 110-fold, resp. There was a cross-resistance to other antimalarial drugs such as mefloquine, artesunate, artemisinine, and chloroquine. The infectivity of the PR line to mice was lower than that of the parent line, indicating that the virulence dropped while the resistance increased.

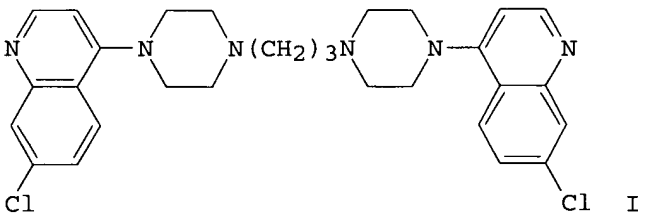
IT **74351-59-0**
RL: BIOL (Biological study)
(resistance to, of piperaquine-resistant Plasmodium berghei)
IT **4085-31-8**
RL: BIOL (Biological study)
(resistance to, of Plasmodium berghei)

L77 ANSWER 45 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1984:401148 HCAPLUS
DOCUMENT NUMBER: 101:1148
TITLE: Effect of prolonged administration of adrenocorticotropic hormone and fluctuations in glucocorticoid production on ultrastructure of rat hepatocytes
AUTHOR(S): Vakulin, G. M.; Shershnev, V. N.
CORPORATE SOURCE: Novosib. Gos. Med. Inst., Novosibirsk, USSR
SOURCE: Eksperimental'naya Meditsina (Riga) (**1984**), 17, 38-46
CODEN: EKMEDL
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB ACTH [9002-60-2] (5 IU/100 g/day for 7 days) injected i.m. into rats increased 11-hydroxycorticosteroid production by the adrenal cortex, the effect being greater after 2 than after 7 days of treatment. The hypercorticism was accompanied by the following ultrastructural changes in hepatocytes: increased mitochondrial volume, decreased mitochondrial surface d. and the number of dense structures in the mitochondria, and increased the nos. of free and bound ribosomes and the volume of glycogen [**900-57-2**]. It had no effect on volume or surface d. of granular endoplasmic reticulum or the volume and number of dense structures of lysosomes and peroxisomes. The effects on the number of dense structures in mitochondria and on the number of dense structures in mitochondria and on ribosomes and glycogen were greater after 7 days than after 2.
IT **900-57-2**
RL: BIOL (Biological study)
(of liver hepatocyte, ACTH chronic administration effect on)

L77 ANSWER 46 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1984:167770 HCAPLUS
DOCUMENT NUMBER: 100:167770
TITLE: Antimalarial effects of hydroxypiperaquine and its phosphate
AUTHOR(S): Li, Yutang; Chen, Lin; Dai, Zurui; Gong, Jianzhang
CORPORATE SOURCE: Second Mil. Med. Coll., Shanghai, 201903, Peop. Rep. China
SOURCE: Zhongguo Yaoli Xuebao (**1984**), 5(1), 57-60
CODEN: CYLPDN; ISSN: 0253-9756
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB Both hydroxypiperaquine [**74351-59-0**] and its phosphate [**89871-82-9**] were effective against chloroquine-resistant Plasmodium berghei in mice, and showed similar reduction rates against P. cynomolgi in monkeys.
IT **74351-59-0 74351-60-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antimalarial activity of)

L77 ANSWER 47 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1984:61601 HCAPLUS
DOCUMENT NUMBER: 100:61601
TITLE: Antihistaminic effect of piperaquine
AUTHOR(S): Fu, Dingyi; Cao, Lihua; Zhu, Lisha; Ma, Xiuxia
CORPORATE SOURCE: Dep. Pharmacol., Tangshan Min. Med. Coll., Tangshan, 063013, Peop. Rep. China
SOURCE: Zhongguo Yaoli Xuebao (**1983**), 4(4), 287-9
CODEN: CYLPDN; ISSN: 0253-9756
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
GI



I

AB Piperaquine (I) [**4085-31-8**] had antihistaminic action in tests in vivo and in vitro; this action appeared to be competitive with histamine. The pA2 of I in antagonizing histamine-induced contractions of the isolated guinea pig ileum was 5.4.

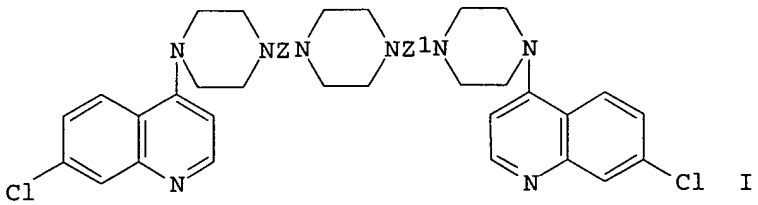
IT **4085-31-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antihistaminic activity of)

L77 ANSWER 48 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1984:61434 HCAPLUS
DOCUMENT NUMBER: 100:61434
TITLE: Experimental therapy with 7 antimalarials in mice infected with pyronaridine-resistant Plasmodium berghei
AUTHOR(S): Chen, Keyong; Lin, Baoying; Zhang, Jiaxun; Shao, Baoruo
CORPORATE SOURCE: Inst. Parasit. Dis., Chin. Acad. Med. Sci., Shanghai, 200025, Peop. Rep. China
SOURCE: Zhongguo Yaoli Xuebao (**1983**), 4(4), 269-73
CODEN: CYLPDN; ISSN: 0253-9756
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

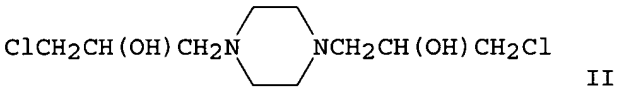
AB A pyronaridine [74847-35-1]-resistant strain of P. berghei in mice was cross-resistant to chloroquine [54-05-7], piperaquine [**4085-31-8**], quinine [130-95-0], and quinacrine [83-89-6] but sensitive to pyrimethamine [58-14-0] and sulfadoxine [2447-57-6]; the ED50 values of the latter 2 drugs were 52.2 and 0.67 mg/kg/day for 3 days, resp. Artemisin [481-05-0], with an ED50 of 1034 mg/kg/day for 3 days, was intermediate. Combined treatment with pyrimethamine plus sulfadoxine had a potentiating effect.

IT **4085-31-8**
RL: BIOL (Biological study)
(Plasmodium berghei resistant to pyronaridine response to)

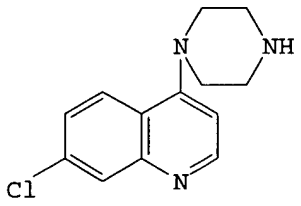
L77 ANSWER 49 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1983:453705 HCAPLUS
DOCUMENT NUMBER: 99:53705
TITLE: Studies on synthetic antimalarials. VI. Synthesis and antimalarial activity of some tripiperaquines
AUTHOR(S): Xu, Deyu; Chen, Xiong; Yin, Xiangsheng; Ning, Xiaomin
CORPORATE SOURCE: Fac. Pharm., 2nd. Mil. Med. Coll., Shanghai, Peop. Rep. China
SOURCE: Yaoxue Xuebao (**1983**), 18(1), 20-4
CODEN: YHHPAL; ISSN: 0513-4870
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
GI



I



II



III

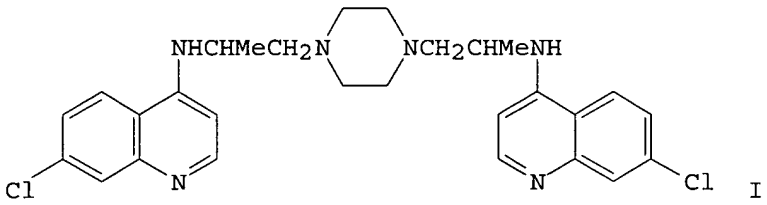
AB Tripiperaquine derivs. [I; Z, Z1 = (CH2)n where n = 2, 3, 4; CH2CHMe, CH2CHRCH2 where R = Cl, HO, PrCO2] were prepared and showed antimalarial activity at 3 mg/kg. Thus, 0.7 mol glycidyl chloride was added to a solution of 0.3 mol piperazine in EtOH at 40-50° and refluxed to give 87.0% II, which (0.01 mol) was refluxed with 0.021 mol III and 2.5 g Et3N in EtOH to give 79% I [Z = Z1 = CH2CH(OH)CH2].

IT **53658-96-1P 86486-21-7P 86486-22-8P**
86486-23-9P 86486-24-0P 86486-26-2P
86486-28-4P 86486-29-5P 86486-30-8P
86486-32-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and antimalarial activity of)

IT **837-52-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with bis(chlorohydroxypropyl)piperazine)

L77 ANSWER 50 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1983:212709 HCAPLUS

DOCUMENT NUMBER: 98:212709
TITLE: Dichloroquinazine (a 4-aminoquinoline) effective in vitro against chloroquine-resistant Plasmodium falciparum
AUTHOR(S): Le Bras, J.; Deloron, P.; Charmot, G.
CORPORATE SOURCE: Inst. Trop. Med. Epidemiol., Hop. Claude Bernard, Paris, 75019, Fr.
SOURCE: Lancet (**1983**), 1(8314-5), 73-4
CODEN: LANCAO; ISSN: 0023-7507
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB The activity of dichloroquinazine (I) against a P. falciparum strain isolated from malarial patients was studied in continuous culture. I was more potent than chloroquine, mefloquine, piperaquine, and 14153 RP. The median inhibitory concentrate (IC50) of I was 16-37 nmol/L, vs. 1100, 40-100, 62-94, and 66-140 nmol/L for chloroquine, mefloquine, piperaquine, and 14153 RP, resp. After long-term cultivation without drug pressure, 8 strains of P. falciparum became resistant to chloroquine but maintained a high sensitivity to I.

IT **4085-31-8**
RL: BIOL (Biological study)
(Plasmodium falciparum susceptibility to, dichloroquinazine in relation to)

L77 ANSWER 51 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1983:174530 HCAPLUS
DOCUMENT NUMBER: 98:174530
TITLE: Study on the method for detecting DNA excision repair of human peripheral blood lymphocytes exposed to chemical carcinogens
AUTHOR(S): Hong, Changfu; Yu, Manqing; Wang, Shouren; Yu, Shuqing; Yu, Yongdan
CORPORATE SOURCE: Zhejiang Inst. Public Hyg., Peop. Rep. China
SOURCE: Shengwu Huaxue Yu Shengwu Wuli Jinzhan (**1983**), 49, 47-9, 6, 73
CODEN: SHYCD4; ISSN: 1000-3282
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB Cultured human peripheral blood lymphocytes were treated with hydroxyurea, mixed with test compds. (10-3-10-7M) and [3H]thymidine (1 μCi/mi) and the mixts. incubated for 6 h and centrifuged. The precipitate was treated with 3% AcOH, mixed with 1 mM EDTA, and the resultant mixture centrifuged to give cells, which were ruptured by treatment with NaSCN at room temperature for 16 h.

After adding DNA (0.1 mg/mL) as carrier, the solution was treated with 30% cold Cl3CCO2H at 4° for 30 min, centrifuged and the precipitate hydrolyzed with 0.5N HCLO4 at 80° for 60 min. After centrifugation, the

supernatant was counted with a scintillation counter for the determination of carcinogen-induced DNA repair. Thus, 2,7-diaminofluorene [525-64-4], Me methanesulfonate [66-27-3] and MNNG [70-25-7] showed pos. results, whereas Na2S2O5, fenitrothion [122-14-5], piperaquine phosphate [**85547-56-4**], biphenylamine [41674-04-8] and NaN3 showed neg. results.

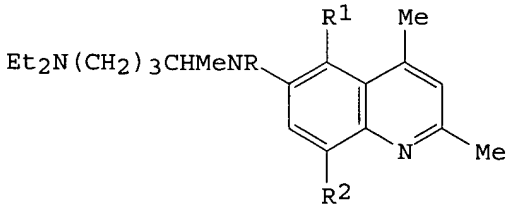
IT **85547-56-4**
RL: BIOL (Biological study)
(DNA repair by human lymphocytes induction by, carcinogenicity in relation to)

L77 ANSWER 52 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1983:100808 HCAPLUS
DOCUMENT NUMBER: 98:100808
TITLE: Studies on piperaquine as long-acting antimalarial drug against Plasmodium berghei
AUTHOR(S): Zhu, Dingqiu; Dai, Zurui; Li, Jincai; Jiang, Zengkang
CORPORATE SOURCE: Dep. Parasitol., Second Mil. Med. Coll., Shanghai, Peop. Rep. China
SOURCE: Yaoxue Xuebao (**1982**), 17(12), 894-8
CODEN: YHHPAL; ISSN: 0513-4870
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

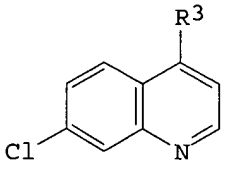
AB The antimalarial action of piperaquine (I) [**83764-65-2**] was examined in mice infected with P. berghei. The duration of its protection against malaria was directly related to the dose administered. At 50 and 200 mg/kg for 3 consecutive days, the drug provided complete protection for 15 and 60 days, resp., against challenge with the parasite. Piperaquine is also a fairly good schizonticide, as it cleared the mice of the asexual blood parasites within 72 h after administration of 12.5 mg (base)/kg for 3 consecutive days. It appears that the drug is more effective and less toxic than chloroquine.

IT **4085-31-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antimalarial activity of)

L77 ANSWER 53 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1983:71886 HCAPLUS
DOCUMENT NUMBER: 98:71886
TITLE: Antimalarial 6-aminoquinolines. XV. The 6- and 4-aminoquinolines with tertiary basic alkylated amino groups
AUTHOR(S): Dann, O.; Steuding, W.; Lisson, K. G.; Seidel, H. R.; Fink, E.; Nickel, P.
CORPORATE SOURCE: Inst. Pharm. Lebensmittelchem., Univ. Erlangen-Nuernberg, Erlangen, Fed. Rep. Ger.
SOURCE: Arzneimittel-Forschung (**1982**), 32(10), 1219-23
CODEN: ARZNAD; ISSN: 0004-4172
DOCUMENT TYPE: Journal
LANGUAGE: German
GI



I, R=H
II, R=Ac
III, R=$COCH_2CH_2CO_2Me$
IV, R=Et
V, R=$(CH_2)_4OH$

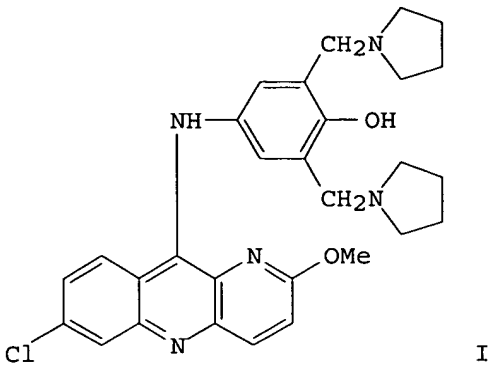


VI

AB Antimalarial 6-aminoquinolines I (R1 = MeO, R2 = MeO, H; R1 = H, R2 = MeO) were acylated to give II (R's the same) and III (R1 = R2 = MeO) and the products reduced with LiAlH4 to give alkylated derivs. IV (R's as for I) and V (R1 = R2 = MeO), to study the influence of a tertiary aromatic 6-amino group on antimalarial activity and toxicity. Treating phenoxyquinoline VI (R3 = PhO) with the appropriate amines gave VI [R3 = 4-methyl-1-piperazinyl, morpholino, NMeCHMe(CH2)3NEt2, NEt(CH2)4NEt2] with tertiary aromatic 4-amino groups to study the influence of such a variation on the biol. activity of the 4-aminoquinolines. The N-alkylated derivs. IV (R's as for I), V (R1 = R2 = MeO), and VI [R3 = NMeCHMe(CH2)3NEt2, NEt(CH2)4NEt2] were active against malaria.

IT **84594-63-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

L77 ANSWER 54 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1983:208 HCAPLUS
DOCUMENT NUMBER: 98:208
TITLE: Development of pyronaridine-resistance in Plasmodium berghei
AUTHOR(S): Shao, Baoruo; Ye, Xiuyu; Zheng, Hao
CORPORATE SOURCE: Inst. Parasit. Dis., Chinese Acad. Med. Sci., Shanghai, Peop. Rep. China
SOURCE: Yaoxue Xuebao (**1982**), 17(8), 566-71
CODEN: YHHPAL; ISSN: 0513-4870
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
GI



I

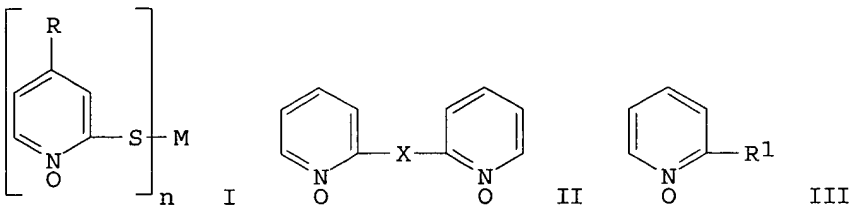
AB A pyronaridine (I) [74847-35-1]-resistant line of P. berghei was developed in mice. The virulence of the I-resistant line was much lower than that of its parent line. The sensitivity of the I-resistant line to 6 erythrocytic schizontocides (chloroquine [54-05-7], piperaquinoline [**83764-65-2**], amopyroquine [550-81-2], M-6407 [83764-57-2], mepacrine [83-89-6], and quinghaosu [63968-64-9]) was also decreased, indicating the presence of cross-resistance. I sensitivity could be restored by 5 passages without I treatment.

IT **4085-31-8**
RL: BIOL (Biological study)
(Plasmodium berghei pyronaridine-resistant strain cross-resistance to)

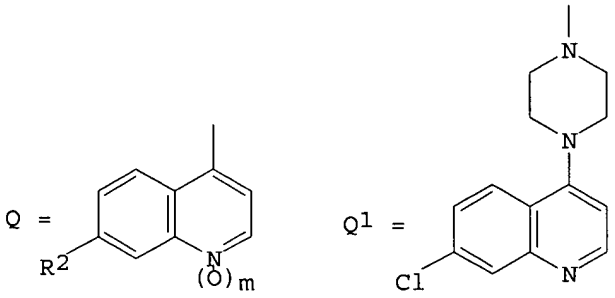
L77 ANSWER 55 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	1982:615876 HCAPLUS
DOCUMENT NUMBER:	97:215876
TITLE:	Synthesis and antimalarial activities of some zincpolyanemine derivatives
AUTHOR(S):	Xu, Bingxiang; Han, Gongyu; Meng, Lining; Chen, Lin; Dai, Zurui; Ma, Zhiming
CORPORATE SOURCE:	2nd Univ. Mil. Med., Peop. Rep. China
SOURCE:	Yaoxue Tongbao (**1982**), 17(5), 302-3 CODEN: YHTPAD; ISSN: 0512-7343
DOCUMENT TYPE:	Journal
LANGUAGE:	Chinese

GI



I II III

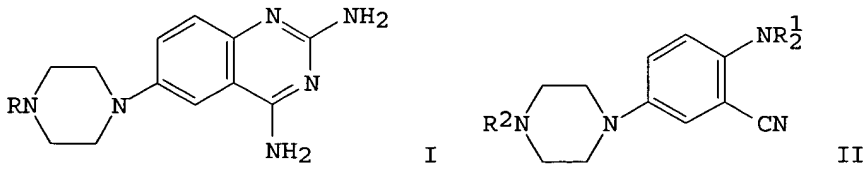


Q = Q1 =

AB Zinepolyanemine analogs I (R = H, Me; M = Na, Li, Mg, Ca, Fe, Al; n = valence of M), II [X = SS, S (CH2)3S, SO2NHNHSO2, OCuO], 3[R1 = AcNH, SH, SCH2CONHNH2, HO2CCH2S, QS (m = 0, R2 = Cl), Q1], QSH (m = 1, R2 = H), etc., were prepared (no synthetic procedures given). Several have higher antimalarial activity and lower toxicity than zincpolyanemine.

IT **83646-07-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and antimalarial activity of)

L77 ANSWER 56 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1982:509953 HCAPLUS
DOCUMENT NUMBER: 97:109953
TITLE: Studies on antimalarials. III. Synthesis and antimalarial effects of some derivatives of 2,4-diamino-6-substituted piperazinylquinazolines
AUTHOR(S): Zhang, Xiuping; Li, Guangyun; Dai, Zurui; Qian, Yongle; Chen, Lin
CORPORATE SOURCE: Shanghai Inst. Pharm. Ind. Res., Shanghai, Peop. Rep. China
SOURCE: Yaoxue Xuebao (**1981**), 16(6), 415-24
CODEN: YHHPAL; ISSN: 0513-4870
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
GI



I II

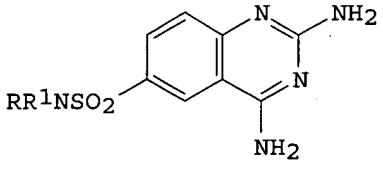
AB Quinazoline derivs. (I; R = alkyl, PhCH2, MeSO2, etc.), antimalarials at 20-200 mg/kg and 0.01% concentration in mice and chickens, resp., were prepared Thus, a mixture of 0.1 mol 5,2-Cl(O2N)C6H3CN and 0.45 mol piperazine·6H2O in MeOCH2CH2OH was heated 5 min at 60° to give 90.5% II (R12 = O, R2 = H), which (0.042 mol) was reduced with SnCl2 in HCl at <30° to give 54.1% II (R1 = R2 = H). Cyclocondensation of 0.1 mol II·HCl (R1 = H, R2 = pentyl) with 0.1 mol cyanoguanidine at 190-5° gave 39.8% I (R = pentyl). Similarly prepared were 11 addnl. I.

IT **82596-72-3P 82596-76-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and antimalarial activity of)

IT **82596-53-0P 82596-54-1P 82596-55-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclocondensation of, with cyanoguanidine)

IT **82596-33-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reduction of)

L77 ANSWER 57 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1982:122726 HCAPLUS
DOCUMENT NUMBER: 96:122726
TITLE: Studies on antimalarial agents. VI. Synthesis and their antimalarial activities of 2,4-diamino-6-substituted-aminosulfonylquinazoline derivatives
AUTHOR(S): Zhang, Xiuping; Shen, Defu; Zhang, Xiuju; Chen, Lin; Dai, Zurui; Shu, Kangquan
CORPORATE SOURCE: Shanghai Inst. Pharm. Ind. Res., Shanghai, Peop. Rep. China
SOURCE: Yaoxue Xuebao (**1981**), 16(11), 877-80
CODEN: YHHPAL; ISSN: 0513-4870
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
GI



I

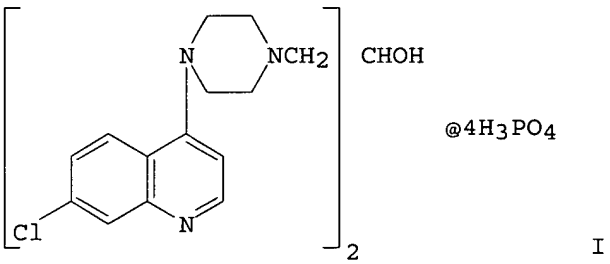
AB Sixteen quinazolinesulfonamides I [NRR1 = alkylamino, 1-pyrrolidinyl, piperidino (II), morpholino, etc.] were prepared by amidation of 2,4-diaminoquinazoline-6-sulfonyl chloride. II showed pronounced prophylactic activity against Plasmodium yoelii.

IT **837-52-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(amidation of quinazolinesulfonyl chloride by)

IT **81099-88-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and antimalarial activity of)

L77 ANSWER 58 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1980:461697 HCAPLUS
DOCUMENT NUMBER: 93:61697
TITLE: Therapeutic effectiveness of "Antisilicon Number 1" (1,3-bis[4-(7-chloro-4-quinonyl)piperazinyl]-2-propanol tetraphosphate) in treatment of silicosis and anthracosis
CORPORATE SOURCE: Shensi No. 1 Antisilicon Coordination Unit, Peop. Rep. China
SOURCE: Shaanxi Xinyiyao (**1979**), 8(12), 14-19
CODEN: SHIYDO; ISSN: 0253-9853
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
GI



I

AB Antisilicon Number 1 (I) [**74351-60-3**] was synthesized and used in the treatment of silicosis and anthracosis. In animal expts., I (200 mg/kg, intragastrically) administered to rats effectively controlled exptl. induced silicosis. Of 297 cases of silicosis or anthracosis tested, conditions of 28 patients were markedly improved and those of 262 patients were stabilized. Serum celuroplasmin levels were markedly lowered compared to those found in patients prior to treatment. However, side effects such as thirst, nausea, and headache were found in some patients after I treatment.
IT **74351-60-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, anthrocosis and silicosis treatment with)

L77 ANSWER 59 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1976:99536 HCAPLUS
DOCUMENT NUMBER: 84:99536
TITLE: Tripiperaquine (M 1020)
CORPORATE SOURCE: Laboratory of Malaria Research, Shanghai Institute of Parasitic Diseases, Shanghai, Peop. Rep. China
SOURCE: Zhonghua Yixue Zazhi (Beijing, China) (**1975**), 1(6), 419-24
CODEN: CHHTAT; ISSN: 0376-2491
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB A single dose of 500 mg M 1020 (I) [**53658-96-1**]/kg (orally) had a suppressive prophylactic effect against trophozoite-induced Plasmodium berghei infection in mice which lasted as long as 50 days. In monkeys

infected with trophozoite-induced P. cynomolgi, a single oral dose of 100 mg tripiperaquine phosphate [**57875-52-2**]/kg afforded a significant suppressive effect for 30 days. I toxicity studies in mice, rabbits, dogs, and monkeys suggested that these animals could tolerate a dose 5-40 times greater than adult man. In monkeys, the fanasil-pyrimethamine-tripiperaquine mixture [**53734-41-1**] was more effective against faliciparum malaria than any of the drugs given alone. In patients, the fanasil-pyrimethamine-tripiperaquine phosphate mixture [**57973-65-6**] given in 2 doses was as effective as chloroquine [54-05-7] against falciparum and vivax malaria.

IT **53658-96-1 53734-41-1 57875-52-2**
57973-65-6
RL: BIOL (Biological study)
(antimalarial)

L77 ANSWER 60 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1975:51487 HCAPLUS
DOCUMENT NUMBER: 82:51487
TITLE: Tripiperaquine (M 1020)
CORPORATE SOURCE: Laboratory of Malaria Research, Shanghai Inst. Parasit. Dis., Shanghai, Peop. Rep. China
SOURCE: Zhonghua Yixue Zazhi (Beijing, China) (**1974**), 54(8), 488-92
CODEN: CHHTAT; ISSN: 0376-2491
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
GI For diagram(s), see printed CA Issue.
AB M 1020 [1,4-bis[2-[(7-chloroquinolin-4-yl)piperazino]ethyl]piperazine](I) [**53658-96-1**] was less toxic and had a longer action, prophylactically and therapeutically, than chloroquine [54-05-7] against the rodent parasite Plasmodium berghei in mice and the simian parasites P. inui and P. cynomolgi in rhesus monkeys. M 1020-fanasil-pyrimethamine mixture (I complex) [**53734-41-1**] had greater effects than I alone. A single oral dose of I complex or 13228RP complex [53789-39-2] decreased the incidence of malaria 65%. The prophylactic effect of a single oral dose of I complex on P. falciparum lasted 30 days, while on P. vivax it persisted only 15 days.

IT **53658-96-1**
RL: BIOL (Biological study)
(antimalarial)

IT **53734-41-1**
RL: BIOL (Biological study)
(antimalarial, tripiperaquine in relation to)

L77 ANSWER 61 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1971:435658 HCAPLUS
DOCUMENT NUMBER: 75:35658
TITLE: Antimalarials. "Distal" hydrazine derivatives of 7-chloroquinoline
AUTHOR(S): Singh, Tara; Hoops, John F.; Biel, John H.; Hoya, Wallace K.; Stein, Robert George; Cruz, Deanna R.
CORPORATE SOURCE: Res. Lab., Aldrich Chem. Co., Inc., Milwaukee, WI, USA
SOURCE: Journal of Medicinal Chemistry (**1971**), 14(6), 532-5
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB 7-Chloroquinolines (I) containing a hydrazine feature in the side chain attached at position 4, were prepared from 4,7-dichloroquinoline and

7-chloro-4-(3-bromo-1-methylpropylamino)quinoline by reacting with the required hydrazine, and were tested for the antimalarial activity against Plasmodium berghei in mice. 1,4-Bis(7-chloro-4-quinolylamino)-piperazine was the best, in which the end NH2 was substituted by a 2nd mol. of 7-chloroquinoline. It showed curative activity at 40 mg/kg, i.p., without toxicity even up to the maximum dose of 640 mg/kg. The I with a distal hydrazine, excluding active 1-[2-(7-chloro-4-quinolinylamino) - 2 - methylethyl] - 1 - methylhydrazine, were inactive, but were highly toxic. The I having a hydrazinium bromide feature, although found curative, were also quite toxic.

IT **32863-63-1P 32863-64-2P 32863-65-3P**
32863-66-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

L77 ANSWER 62 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1971:125372 HCAPLUS
DOCUMENT NUMBER: 74:125372
TITLE: Antimalarials. 7-Chloro-4-(substituted amino)quinolines
AUTHOR(S): Singh, Tara; Stein, Robert George; Hoops, John F.; Biel, John H.; Hoya, Wallace K.; Cruz, Deanna R.
CORPORATE SOURCE: Res. Lab., Aldrich Chem. Co., Inc., Milwaukee, WI, USA
SOURCE: Journal of Medicinal Chemistry (**1971**), 14(4), 283-6
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB Forty-one 7-chloro-4-(substituted amino)quinolines were prepared from 4,7-dichloroquinoline and tested for antimalarial activity against Plasmodium berghei in mice. Of 27 active compds., 7-chloro-4-[(1-ethyl-3-piperidyl)-amine]quinoline (I) and 7-chloro-4-[[4-(benzyl-2-propynylamino]-2-butyl]amino]quinoline (II) were curative antimalarial agents at doses of 80 and 160 mg/kg, i.p.,resp.
IT **837-52-5P 31502-87-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

L77 ANSWER 63 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1970:455947 HCAPLUS
DOCUMENT NUMBER: 73:55947
TITLE: Isoquinolylquinoline derivatives. II. Synthesis of some azaheterocyclic derivatives as possible antispasmodic or amoebicidal agents
AUTHOR(S): Das Gupta, Ahindra C.; Raychaudhuri, Amitabha; Chakravorti, Sibani S.; Basu, U. P.
CORPORATE SOURCE: Bengal Immunity Res. Inst., Calcutta, India
SOURCE: Indian Journal of Chemistry (**1970**), 8(6), 505-8
CODEN: IJOCAP; ISSN: 0019-5103
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB I-VI were prepared I was synthesized by Bischler-Napieralski cyclization of 4-hydroxy-N-(α-methylphenethyl)]-3-quinolinecarboxamide, obtained by the interaction of Et 4-hydroxy-3-quinolinecarboxylate with α-methylphenethylamine. II was obtained by a similar cyclization of 4-hydroxy-N-(2-phenylcyclohexyl)-3-quinolinecarboxamide, obtained by the interaction of ethyl 4-hydroxy-3-quinolinecarboxylate and

2-phenylcyclohexylamine. III-VI were obtained by the interaction of 3-(3,4-dihydro-1-isoquinolyl)-4,7-dichloroquinoline with piperidine, morpholine, 1-carbethoxypiperazine, and 1-benzylpiperazine, resp.

IT **28970-61-8P 28970-62-9P 28970-63-0P**
28970-64-1P 28970-65-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

L77 ANSWER 64 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1966:431383 HCAPLUS
DOCUMENT NUMBER: 65:31383
ORIGINAL REFERENCE NO.: 65:5851h,5852a
TITLE: Fluorometric determination of chloroquine and certain derivatives of 4-aminoquinoline in biological systems
AUTHOR(S): Fournel, Julien
CORPORATE SOURCE: Lab. Rech. Soc. Usines Chim., Rhone-Poulenc, Paris
SOURCE: Ann. Pharm. Franc. (**1966**), 24(2), 133-42
DOCUMENT TYPE: Journal
LANGUAGE: French

AB Chloroquine (I), 1- [4- [(7-chloro-4-quinolyl)amino]pentyl]-4-(7-chloro-4 - quinolyl)piperazine (II),1,4-bis[2-[(7-chloro-4-quinolyl)amino]propyl]-piperazine (III), 1-[2-[(7-chloro-4-quinolyl)amino]propyl]-4-(7-chloro-4-quinolyl)piperazine (IV), and 1-[2-[(7-chloro-4-quinolyl)-amino]propyl]-4-(2-piperidinoethyl)piperazine (V) may be determined fluorometrically in biol. material. I could be extracted with BuOH, the others were 1st oxidized with ferricyanide, and then extracted with BuOH. The excitation and fluorescence peaks and intensity relative to 1 γ/ml. quinine were I 350, 405 mμ, 1.2; II 270, 370 mμ, 0.08; III 360, 425 mμ, 0.9, resp.; I after BuOH extraction 345 ± 5, 385 mμ, 0.3, resp. After oxidn, and BuOH extraction, II-V showed peaks at 345 ± 5 and 385 mμ with a relative intensity of 0.075. The materials were estimated in rat liver and blood.

IT **10547-41-8**, Quinoline, 7-chloro-4-[4-[2-[(7-chloro-4-quinolyl)amino]propyl]-1-piperazinyl]-
(determination in blood and liver)

L77 ANSWER 65 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1965:69264 HCAPLUS
DOCUMENT NUMBER: 62:69264
ORIGINAL REFERENCE NO.: 62:12339b-c
TITLE: N4-Substituted N1-(3-dimethylaminopropyl)piperazines. A new series of compounds active against Trypanosoma cruzi infections in mice
AUTHOR(S): Tomcufcik, Andrew S.; Hewitt, Redginal I.; Fabio, Paul F.; Hoffman, Arlene M.; Entwistle, Joseph
CORPORATE SOURCE: Am. Cyanamid Co., Pearl River, NY
SOURCE: Nature (London, United Kingdom) (**1965**), 205(4971), 605-6
CODEN: NATUAS; ISSN: 0028-0836
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Twelve N4-substituted N1-(3-dimethylaminopropyl)piperazines were prepared and screened for chemotherapeutic activity against the B strain of Trypanosoma cruzi infections in mice. Six-to 8-week-old mice exptl. infected were given the test compds. in the diet on days 6-12 post-inoculation and the survival time of treated mice was compared with the survival time of untreated mice. Activity of the compds. was unaffected when they were given by gavage or by subcutaneous or intraperitoneal injection. While the parent compound was completely inactive in dosage levels up to 512 mg./kg./day, the 4-pyridyl, 7-chloro-4-quinolyl, 4-acetamidophenyl, and the 2-phenyl-20-1,2,3-

triazole-4-carbonyl derivs., in decreasing order of activity, effectively prolonged the survival of the infected mice and increased the number of survivors. The 4-acetamidophenyl derivative was much more effective than furaltadone and primaquine against T. cruzi infections.

IT **298-78-2**, Quinoline, 7-chloro-4-[4-[3-(dimethylamino)propyl]-1-piperazinyl]-
(in Trypanosoma cruzi infestation treatment)

L77 ANSWER 66 OF 66 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1964:425394 HCAPLUS
DOCUMENT NUMBER: 61:25394
ORIGINAL REFERENCE NO.: 61:4349e-g
TITLE: Further investigations of heterocyclic alkylating agents
AUTHOR(S): Preston, Robert K.; Peck, Richard M.; Breuninger, Evelyn R.; Miller, Ann J.; Creech, Hugh J.
CORPORATE SOURCE: Inst. for Cancer Res., Philadelphia, PA
SOURCE: Journal of Medicinal Chemistry (**1964**), 7(4), 471-80
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB The exceptional antitumor and mutagenic activities displayed by a quinacrine derivative of a monofunctional N mustard, 2-methoxy-6chloro-9-[3-(ethyl-2-chloroethyl)aminopropylamino] acridine, led to the synthesis of 50 addnl. mono- and difunctional analogs of acridine, quinoline, and quinazoline. The acridine nucleus was found to exert a pronounced activating influence on the N mustard moiety. On a molar basis, the "half-mustard," 2-methoxy-9-[3-(ethyl-2-chloroethyl)aminopropylamino] acridine dihydrochloride was considerably more effective against the Ehrlich ascites tumor than methylbis(2-chloroethyl)amine hydrochloride; the corresponding bis analog was even more potent. Substitution of a 6-chloro group into 2-methoxyacridine decreased the molar activities of the mono and bis mustards. Several monofunctional N mustards of quinazoline and quinoline displayed moderate antitumor activity, but only at high molar dosages; other closely related analogs were inactive. The relationships between the chemical structures and antitumor activities of the compds. are presented.

IT **93987-83-8**, 1-Piperazineethanol, 4-(7-chloro-4-quinolyl)-, dihydrochloride **94026-62-7**, Quinoline, 7-chloro-4-[4-(2-chloroethyl)-1-piperazinyl]-, dihydrochloride
(preparation of)

=> select hit rn l77 1-66
E1 THROUGH E86 ASSIGNED

=> fil reg
FILE 'REGISTRY' ENTERED AT 20:47:41 ON 10 SEP 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 8 SEP 2005 HIGHEST RN 862771-58-2
DICTIONARY FILE UPDATES: 8 SEP 2005 HIGHEST RN 862771-58-2

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

```
**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,    *
* effective March 20, 2005.  A new display format, IDERL, is now     *
* available and contains the CA role and document type information.  *
*                                                                    *
**********************************************************************
```

Structure search iteration limits have been increased. See HELP SLIMITS for details.

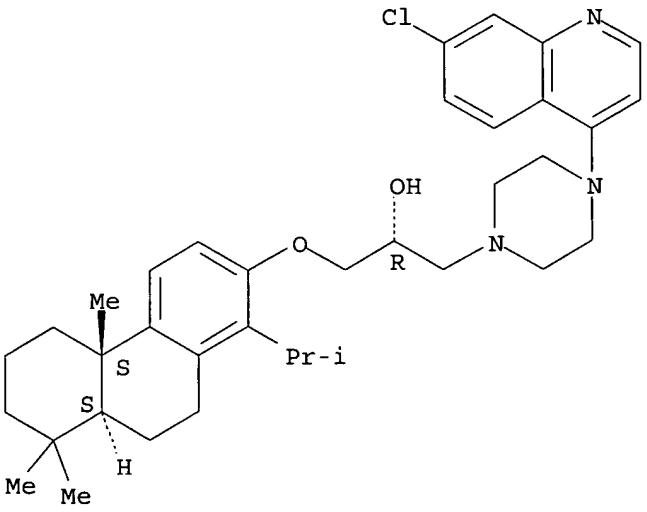
Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

```
=> => d reg l78 1-86
1         RN   660834-27-5  REGISTRY
2         RN   509149-21-7  REGISTRY
3         RN   215592-28-2  REGISTRY
4         RN   205258-54-4  REGISTRY
5         RN   205255-54-5  REGISTRY
6         RN   199444-81-0  REGISTRY
7         RN   199444-80-9  REGISTRY
8         RN   161467-85-2  REGISTRY
9         RN   161467-84-1  REGISTRY
10        RN   161467-83-0  REGISTRY
11        RN   161467-82-9  REGISTRY
12        RN   149225-73-0  REGISTRY
13        RN   149144-34-3  REGISTRY
14        RN   147587-90-4  REGISTRY
15        RN   114282-73-4  REGISTRY
16        RN   114260-08-1  REGISTRY
17        RN   114260-07-0  REGISTRY
18        RN   114260-06-9  REGISTRY
19        RN   114260-05-8  REGISTRY
20        RN   114260-04-7  REGISTRY
21        RN   114260-03-6  REGISTRY
22        RN   114260-02-5  REGISTRY
23        RN   114260-01-4  REGISTRY
24        RN   114260-00-3  REGISTRY
25        RN   114259-99-3  REGISTRY
26        RN   114259-98-2  REGISTRY
27        RN   104692-85-5  REGISTRY
28        RN   104668-07-7  REGISTRY
29        RN   104667-95-0  REGISTRY
30        RN   104667-94-9  REGISTRY
31        RN   103248-83-5  REGISTRY
32        RN   103248-82-4  REGISTRY
33        RN   103248-81-3  REGISTRY
34        RN   103248-80-2  REGISTRY
35        RN   103086-26-6  REGISTRY
36        RN   103086-12-0  REGISTRY
```

```
37        RN    103086-11-9  REGISTRY
38        RN    103086-10-8  REGISTRY
39        RN    103086-09-5  REGISTRY
40        RN    103086-08-4  REGISTRY
41        RN    103085-91-2  REGISTRY
42        RN    100672-05-7  REGISTRY
43        RN     99461-88-8  REGISTRY
44        RN     95560-84-2  REGISTRY
45        RN     94026-62-7  REGISTRY
46        RN     93987-83-8  REGISTRY
47        RN     86486-32-0  REGISTRY
48        RN     86486-30-8  REGISTRY
49        RN     86486-29-5  REGISTRY
50        RN     86486-28-4  REGISTRY
51        RN     86486-26-2  REGISTRY
52        RN     86486-24-0  REGISTRY
53        RN     86486-23-9  REGISTRY
54        RN     86486-22-8  REGISTRY
55        RN     86486-21-7  REGISTRY
56        RN     85547-56-4  REGISTRY
57        RN     84594-63-8  REGISTRY
58        RN     83646-07-5  REGISTRY
59        RN     82596-76-7  REGISTRY
60        RN     82596-72-3  REGISTRY
61        RN     82596-55-2  REGISTRY
62        RN     82596-54-1  REGISTRY
63        RN     82596-53-0  REGISTRY
64        RN     82596-33-6  REGISTRY
65        RN     81099-88-9  REGISTRY
66        RN     74351-60-3  REGISTRY
DR   89871-82-9
67        RN     74351-59-0  REGISTRY
DR   99339-96-5
68        RN     57973-65-6  REGISTRY
69        RN     57875-52-2  REGISTRY
70        RN     53734-41-1  REGISTRY
71        RN     53658-96-1  REGISTRY
72        RN     32863-66-4  REGISTRY
73        RN     32863-65-3  REGISTRY
74        RN     32863-64-2  REGISTRY
75        RN     32863-63-1  REGISTRY
76        RN     31502-87-1  REGISTRY
77        RN     28970-65-2  REGISTRY
78        RN     28970-64-1  REGISTRY
79        RN     28970-63-0  REGISTRY
80        RN     28970-62-9  REGISTRY
81        RN     28970-61-8  REGISTRY
82        RN     10547-41-8  REGISTRY
83        RN      4085-31-8  REGISTRY
DR   83764-65-2
84        RN       900-57-2  REGISTRY
85        RN       837-52-5  REGISTRY
86        RN       298-78-2  REGISTRY


=>
=>
=> d ide can l78 1 2 3 4 5 6 8 12 13 14 15 16 25 27 28 29 31 35 41 42 43 44 45 47
56 57 58 59 65 70 71 72 76 77 82 83 84 85 86
```

L78 ANSWER 1 OF 86 REGISTRY COPYRIGHT 2005 ACS on STN
RN **660834-27-5** REGISTRY
ED Entered STN: 10 Mar 2004
CN 1-Piperazineethanol, 4-(7-chloro-4-quinolinyl)-α-[[[(4bS,8aS)-4b,5,6,7,8,8a,9,10-octahydro-4b,8,8-trimethyl-1-(1-methylethyl)-2-phenanthrenyl]oxy]methyl]-, (αR)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C36 H48 Cl N3 O2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

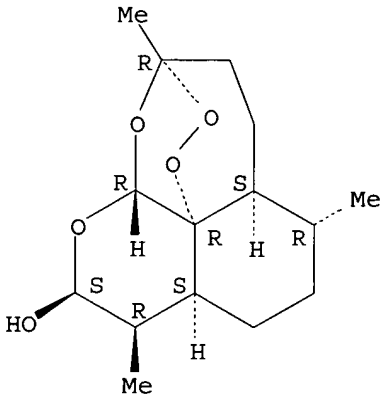
REFERENCE 1: 140:192195

L78 ANSWER 2 OF 86 REGISTRY COPYRIGHT 2005 ACS on STN
RN **509149-21-7** REGISTRY
ED Entered STN: 02 May 2003
CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-ol, decahydro-3,6,9-trimethyl-, (3R,5aS,6R,8aS,9R,10S,12R,12aR)-, mixt. with 4,4'-(1,3-propanediyldi-4,1-piperazinediyl)bis[7-chloroquinoline] and 5-[(3,4,5-trimethoxyphenyl)methyl]-2,4-pyrimidinediamine (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Artecom
FS STEREOSEARCH
MF C29 H32 Cl2 N6 . C15 H24 O5 . C14 H18 N4 O3
CI MXS
SR CA
LC STN Files: BIOSIS, CA, CAPLUS, TOXCENTER

CM 1

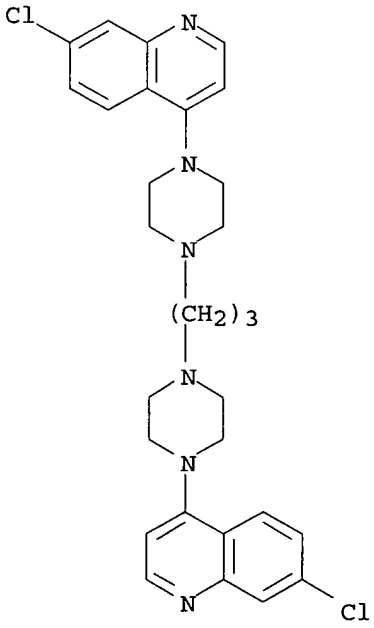
CRN 71939-50-9
CMF C15 H24 O5

Absolute stereochemistry.



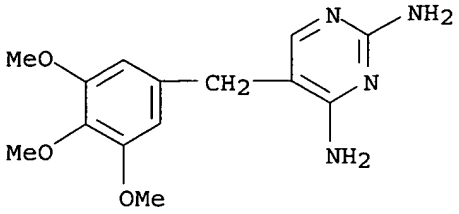
CM 2

CRN 4085-31-8
CMF C29 H32 Cl2 N6



CM 3

CRN 738-70-5
CMF C14 H18 N4 O3

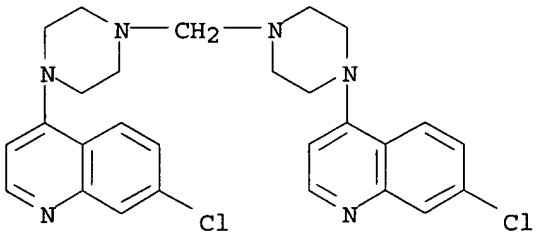


2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:192272

REFERENCE 2: 138:297135

L78 ANSWER 3 OF 86 REGISTRY COPYRIGHT 2005 ACS on STN
RN **215592-28-2** REGISTRY
ED Entered STN: 15 Dec 1998
CN Quinoline, 4,4'-(methylenedi-4,1-piperazinediyl)bis[7-chloro- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C27 H28 Cl2 N6
SR CA
LC STN Files: CA, CAPLUS

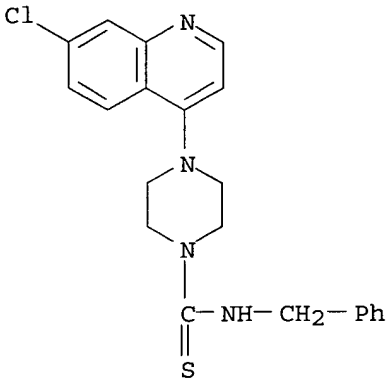


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 129:343400

L78 ANSWER 4 OF 86 REGISTRY COPYRIGHT 2005 ACS on STN
RN **205258-54-4** REGISTRY
ED Entered STN: 07 May 1998
CN 1-Piperazinecarbothioamide, 4-(7-chloro-4-quinolinyl)-N-(phenylmethyl)-(9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C21 H21 Cl N4 S
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPAT2, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

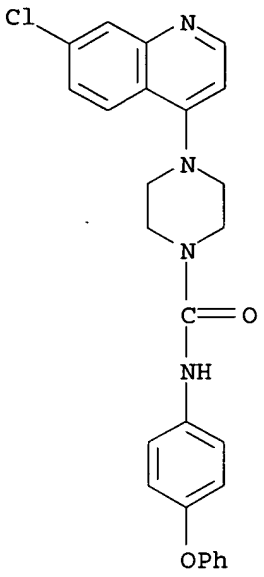
3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:22645

REFERENCE 2: 134:86277

REFERENCE 3: 128:257447

L78 ANSWER 5 OF 86 REGISTRY COPYRIGHT 2005 ACS on STN
RN **205255-54-5** REGISTRY
ED Entered STN: 07 May 1998
CN 1-Piperazinecarboxamide, 4-(7-chloro-4-quinolinyl)-N-(4-phenoxyphenyl)-
(9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C26 H23 Cl N4 O2
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPAT2, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

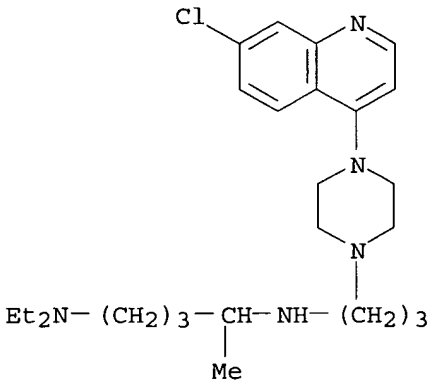
3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:22645

REFERENCE 2: 134:86277

REFERENCE 3: 128:257447

L78 ANSWER 6 OF 86 REGISTRY COPYRIGHT 2005 ACS on STN
RN **199444-81-0** REGISTRY
ED Entered STN: 07 Jan 1998
CN 1,4-Pentanediamine, N4-[3-[4-(7-chloro-4-quinolinyl)-1-piperazinyl]propyl]-N1,N1-diethyl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C25 H40 Cl N5
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

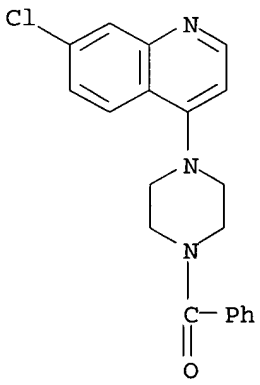


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 128:48119

L78 ANSWER 8 OF 86 REGISTRY COPYRIGHT 2005 ACS on STN
RN **161467-85-2** REGISTRY
ED Entered STN: 14 Mar 1995
CN Piperazine, 1-benzoyl-4-(7-chloro-4-quinolinyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C20 H18 Cl N3 O
SR CA
LC STN Files: CA, CAPLUS, CHEMCATS

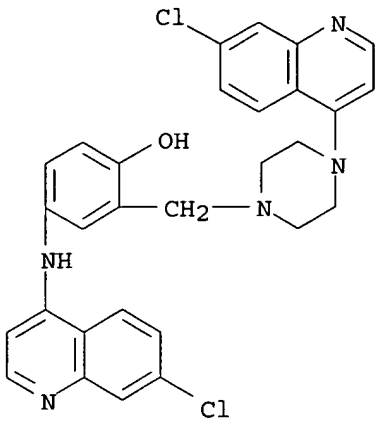


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 122:160450

L78 ANSWER 12 OF 86 REGISTRY COPYRIGHT 2005 ACS on STN

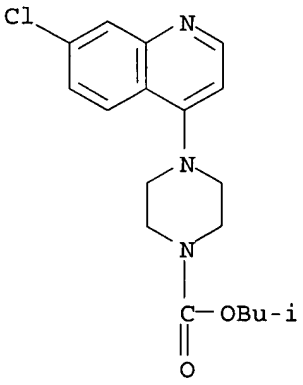


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 108:186530

L78 ANSWER 25 OF 86 REGISTRY COPYRIGHT 2005 ACS on STN
RN **114259-99-3** REGISTRY
ED Entered STN: 07 May 1988
CN 1-Piperazinecarboxylic acid, 4-(7-chloro-4-quinolinyl)-, 2-methylpropyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C18 H22 Cl N3 O2
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

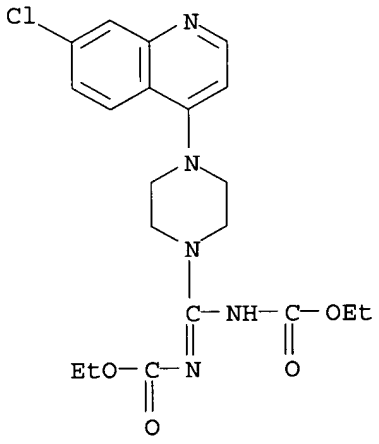
REFERENCE 1: 108:186530

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 118:233972

L78 ANSWER 15 OF 86 REGISTRY COPYRIGHT 2005 ACS on STN
RN **114282-73-4** REGISTRY
ED Entered STN: 07 May 1988
CN Carbamic acid, [[4-(7-chloro-4-quinolinyl)-1-piperazinyl][(ethoxycarbonyl) amino]methylene]-, ethyl ester (9CI) (CA INDEX NAME)
OTHER NAMES:
CN NSC 602122
FS 3D CONCORD
MF C20 H24 Cl N5 O4
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, TOXCENTER
(*File contains numerically searchable property data)

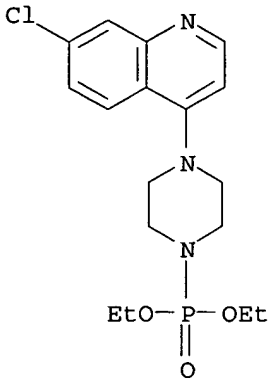


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 108:186530

L78 ANSWER 16 OF 86 REGISTRY COPYRIGHT 2005 ACS on STN
RN **114260-08-1** REGISTRY
ED Entered STN: 07 May 1988
CN Phenol, 4-[(7-chloro-4-quinolinyl)amino]-2-[[4-(7-chloro-4-quinolinyl)-1-piperazinyl]methyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C29 H25 Cl2 N5 O
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, TOXCENTER
(*File contains numerically searchable property data)

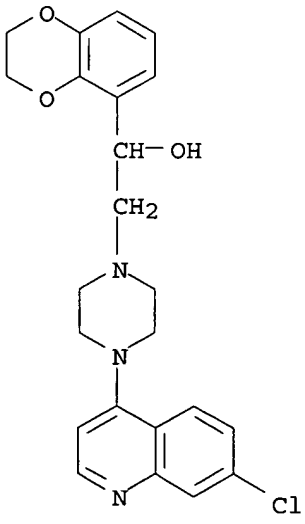


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

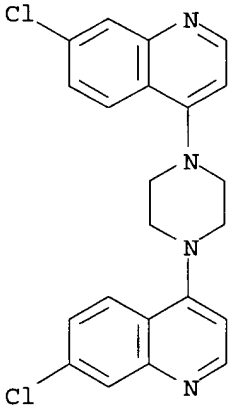
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 119:95665

L78 ANSWER 14 OF 86 REGISTRY COPYRIGHT 2005 ACS on STN
RN **147587-90-4** REGISTRY
ED Entered STN: 14 May 1993
CN 1-Piperazineethanol, 4-(7-chloro-4-quinolinyl)-α-(2,3-dihydro-1,4-benzodioxin-5-yl)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1,4-Benzodioxin, 1-piperazineethanol deriv.
FS 3D CONCORD
MF C23 H24 Cl N3 O3
SR CA
LC STN Files: CA, CAPLUS



RN **149225-73-0** REGISTRY
ED Entered STN: 11 Aug 1993
CN Quinoline, 4,4'-(1,4-piperazinediyl)bis[7-chloro-, tetrahydrochloride (9CI) (CA INDEX NAME)
MF C22 H18 Cl2 N4 . 4 Cl H
SR CA
LC STN Files: CA, CAPLUS
CRN (31502-87-1)



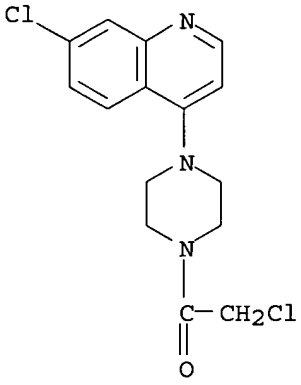
●4 HCl

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 119:95477

L78 ANSWER 13 OF 86 REGISTRY COPYRIGHT 2005 ACS on STN
RN **149144-34-3** REGISTRY
ED Entered STN: 05 Aug 1993
CN Phosphonic acid, [4-(7-chloro-4-quinolinyl)-1-piperazinyl]-, diethyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C17 H23 Cl N3 O3 P
SR CA
LC STN Files: CA, CAPLUS

L78 ANSWER 27 OF 86 REGISTRY COPYRIGHT 2005 ACS on STN
RN **104692-85-5** REGISTRY
ED Entered STN: 18 Oct 1986
CN Piperazine, 1-(chloroacetyl)-4-(7-chloro-4-quinolinyl)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 4-(4-Chloroacetyl-1-piperazinyl)-7-chloroquinoline
FS 3D CONCORD
MF C15 H15 Cl2 N3 O
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, IPA, TOXCENTER
(*File contains numerically searchable property data)



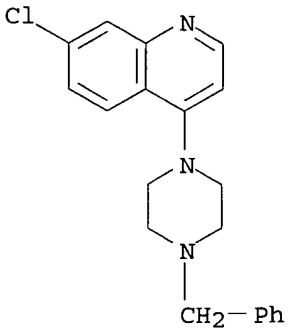
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 108:186530

REFERENCE 2: 105:164484

L78 ANSWER 28 OF 86 REGISTRY COPYRIGHT 2005 ACS on STN
RN **104668-07-7** REGISTRY
ED Entered STN: 11 Oct 1986
CN Quinoline, 7-chloro-4-[4-(phenylmethyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C20 H20 Cl N3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

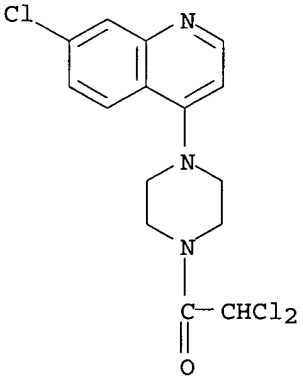


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 105:164484

L78 ANSWER 29 OF 86 REGISTRY COPYRIGHT 2005 ACS on STN
RN **104667-95-0** REGISTRY
ED Entered STN: 11 Oct 1986
CN Piperazine, 1-(7-chloro-4-quinolinyl)-4-(dichloroacetyl)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 4-(4-Dichloroacetyl-1-piperazinyl)-7-chloroquinoline
FS 3D CONCORD
MF C15 H14 Cl3 N3 O
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

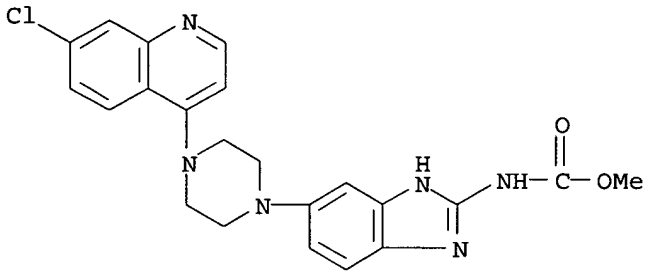


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 105:164484

L78 ANSWER 31 OF 86 REGISTRY COPYRIGHT 2005 ACS on STN
RN **103248-83-5** REGISTRY
ED Entered STN: 19 Jul 1986
CN Carbamic acid, [5-[4-(7-chloro-4-quinolinyl)-1-piperazinyl]-1H-benzimidazol-2-yl]-, methyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C22 H21 Cl N6 O2
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT
(*File contains numerically searchable property data)

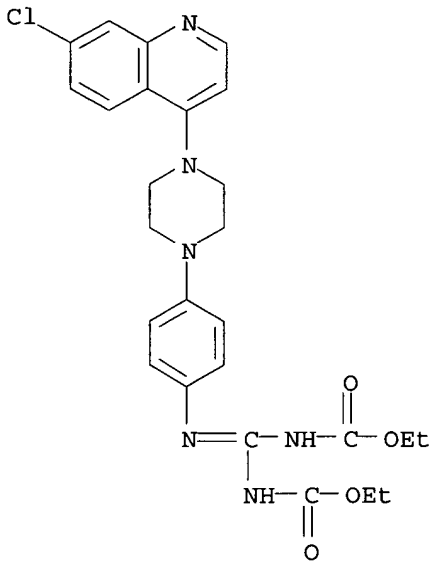


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 105:42720

L78 ANSWER 35 OF 86 REGISTRY COPYRIGHT 2005 ACS on STN
RN **103086-26-6** REGISTRY
ED Entered STN: 04 Jul 1986
CN Carbamic acid, [[4-[4-(7-chloro-4-quinolinyl)-1-piperazinyl]phenyl]carbonimidoyl]bis-, diethyl ester (9CI) (CA INDEX NAME)
MF C26 H29 Cl N6 O4
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT
(*File contains numerically searchable property data)

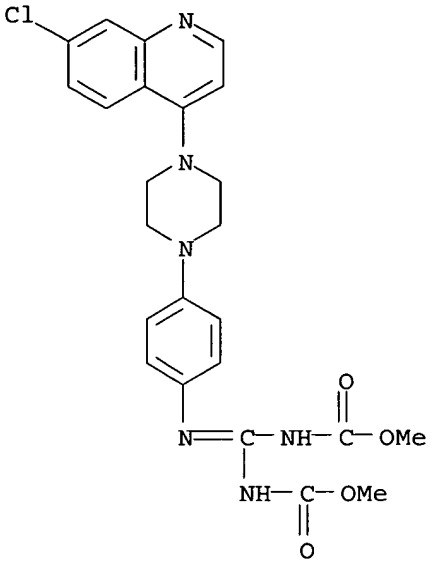


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 105:35178

L78 ANSWER 41 OF 86 REGISTRY COPYRIGHT 2005 ACS on STN
RN **103085-91-2** REGISTRY
ED Entered STN: 04 Jul 1986
CN Carbamic acid, [[4-[4-(7-chloro-4-quinolinyl)-1-piperazinyl]phenyl]carbonimidoyl]bis-, dimethyl ester (9CI) (CA INDEX NAME)
MF C24 H25 Cl N6 O4
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT
(*File contains numerically searchable property data)

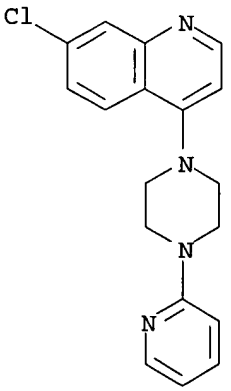


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 105:35178

L78 ANSWER 42 OF 86 REGISTRY COPYRIGHT 2005 ACS on STN
RN **100672-05-7** REGISTRY
ED Entered STN: 08 Mar 1986
CN Quinoline, 7-chloro-4-[4-(2-pyridinyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C18 H17 Cl N4
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT
(*File contains numerically searchable property data)

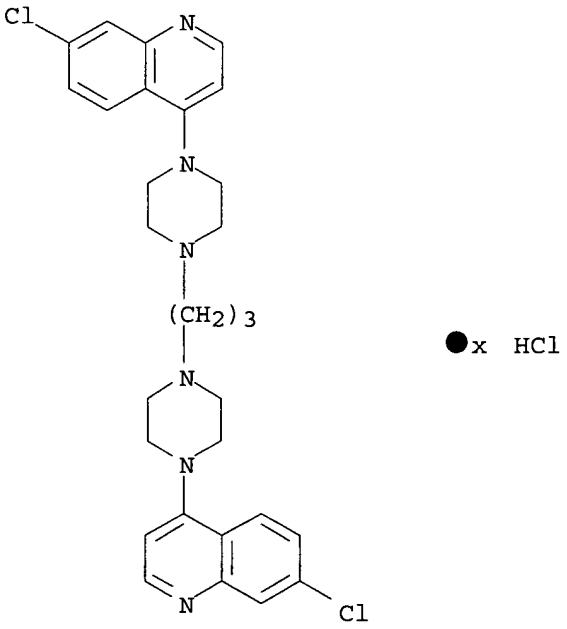


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 104:148706

L78 ANSWER 43 OF 86 REGISTRY COPYRIGHT 2005 ACS on STN
RN **99461-88-8** REGISTRY
ED Entered STN: 15 Dec 1985
CN Quinoline, 4,4'-(1,3-propanediyldi-4,1-piperazinediyl)bis[7-chloro-, hydrochloride (9CI) (CA INDEX NAME)
MF C29 H32 Cl2 N6 . x Cl H
SR CA
LC STN Files: CA, CAPLUS
CRN (4085-31-8)

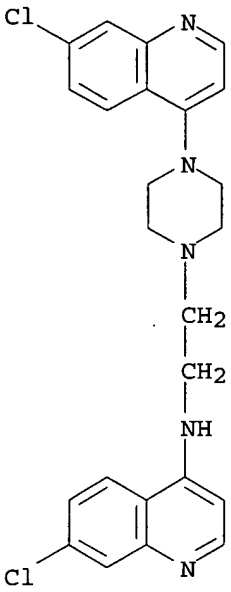


1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 104:3319

L78 ANSWER 44 OF 86 REGISTRY COPYRIGHT 2005 ACS on STN
RN **95560-84-2** REGISTRY
ED Entered STN: 30 Mar 1985
CN 4-Quinolinamine, 7-chloro-N-[2-[4-(7-chloro-4-quinolinyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Quinoline, 7-chloro-4-[4-[2-[(7-chloro-4-quinolyl)amino]ethyl]-1-piperazinyl]- (7CI)
OTHER NAMES:
CN Q 2-11
FS 3D CONCORD

MF C24 H23 Cl2 N5
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES IN FILE CAPLUS (1907 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 142:309855

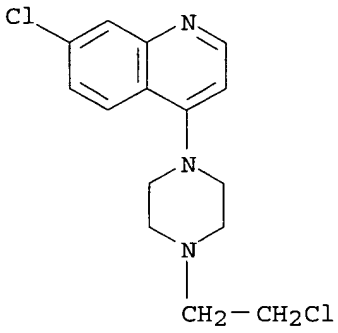
REFERENCE 2: 140:24370

REFERENCE 3: 131:13355

REFERENCE 4: 129:343400

REFERENCE 5: 59:35548

L78 ANSWER 45 OF 86 REGISTRY COPYRIGHT 2005 ACS on STN
RN **94026-62-7** REGISTRY
ED Entered STN: 02 Jan 1985
CN Quinoline, 7-chloro-4-[4-(2-chloroethyl)-1-piperazinyl]-, dihydrochloride (7CI) (CA INDEX NAME)
MF C15 H17 Cl2 N3 . 2 Cl H
LC STN Files: CA, CAOLD, CAPLUS, TOXCENTER
CRN (92645-66-4)



●2 HCl

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

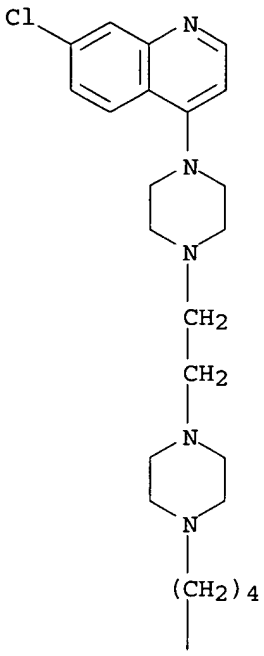
REFERENCE 1: 61:25394

L78 ANSWER 47 OF 86 REGISTRY COPYRIGHT 2005 ACS on STN
RN **86486-32-0** REGISTRY
ED Entered STN: 16 Nov 1984
CN Quinoline, 7-chloro-4-[4-[2-[4-[4-[4-(7-chloro-4-quinolinyl)-1-piperazinyl]butyl]-1-piperazinyl]ethyl]-1-piperazinyl]-, phosphate (1:6) (9CI) (CA INDEX NAME)
MF C36 H46 Cl2 N8 . 6 H3 O4 P
LC STN Files: CA, CAPLUS

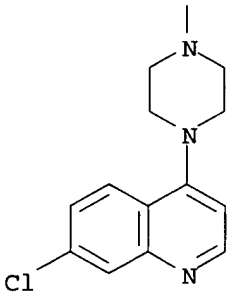
CM 1

CRN 86486-31-9
CMF C36 H46 Cl2 N8

PAGE 1-A

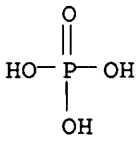


PAGE 2-A



CM 2

CRN 7664-38-2
CMF H3 O4 P



1 REFERENCES IN FILE CA (1907 TO DATE)

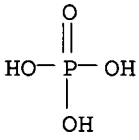
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 99:53705

L78 ANSWER 56 OF 86 REGISTRY COPYRIGHT 2005 ACS on STN
RN **85547-56-4** REGISTRY
ED Entered STN: 16 Nov 1984
CN Quinoline, 4,4'-(1,3-propanediyldi-4,1-piperazinediyl)bis[7-chloro-, phosphate (9CI) (CA INDEX NAME)
MF C29 H32 Cl2 N6 . x H3 O4 P
LC STN Files: CA, CAPLUS, TOXCENTER

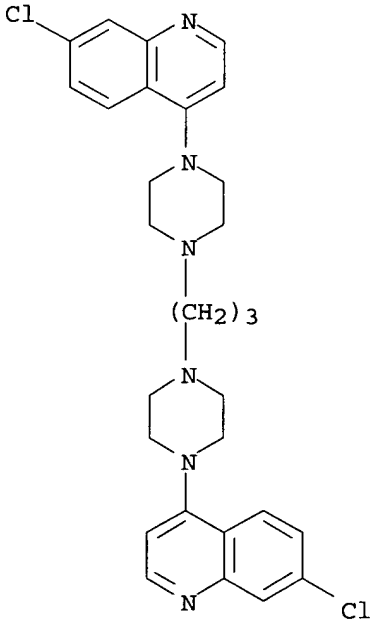
CM 1

CRN 7664-38-2
CMF H3 O4 P



CM 2

CRN 4085-31-8
CMF C29 H32 Cl2 N6



6 REFERENCES IN FILE CA (1907 TO DATE)
6 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:284410

REFERENCE 2: 133:213090

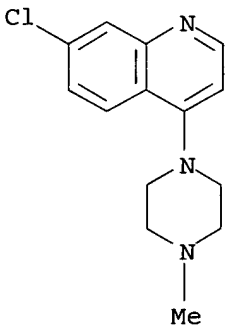
REFERENCE 3: 126:122553

REFERENCE 4: 123:246391

REFERENCE 5: 111:51902

REFERENCE 6: 98:174530

L78 ANSWER 57 OF 86 REGISTRY COPYRIGHT 2005 ACS on STN
RN **84594-63-8** REGISTRY
ED Entered STN: 16 Nov 1984
CN Quinoline, 7-chloro-4-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C14 H16 Cl N3
CI COM
LC STN Files: CA, CAPLUS, CHEMCATS, TOXCENTER

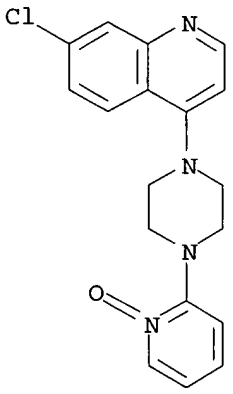


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 98:71886

L78 ANSWER 58 OF 86 REGISTRY COPYRIGHT 2005 ACS on STN
RN **83646-07-5** REGISTRY
ED Entered STN: 16 Nov 1984
CN Quinoline, 7-chloro-4-[4-(1-oxido-2-pyridinyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Quinoline, 7-chloro-4-[4-(2-pyridinyl)-1-piperazinyl]-, N-oxide
FS 3D CONCORD
MF C18 H17 Cl N4 O
LC STN Files: CA, CAPLUS, TOXCENTER



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

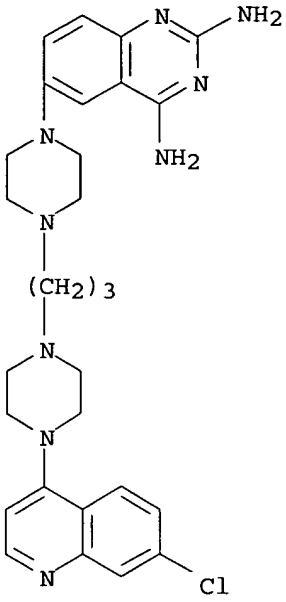
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 97:215876

L78 ANSWER 59 OF 86 REGISTRY COPYRIGHT 2005 ACS on STN
RN **82596-76-7** REGISTRY
ED Entered STN: 16 Nov 1984
CN 2,4-Quinazolinediamine, 6-[4-[3-[4-(7-chloro-4-quinolinyl)-1-piperazinyl]propyl]-1-piperazinyl]-, tetrakis(4-methylbenzenesulfonate) (9CI) (CA INDEX NAME)
MF C28 H34 Cl N9 . 4 C7 H8 O3 S
LC STN Files: CA, CAPLUS

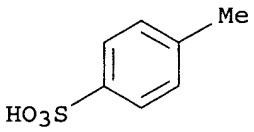
CM 1

CRN 82596-75-6
CMF C28 H34 Cl N9



CM 2

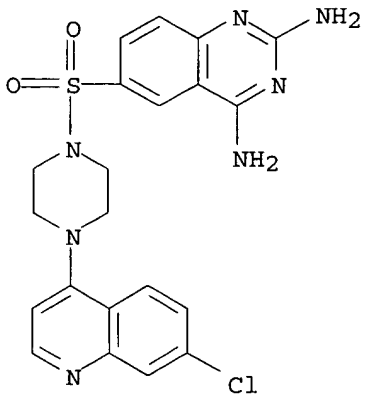
CRN 104-15-4
CMF C7 H8 O3 S



1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 97:109953

L78 ANSWER 65 OF 86 REGISTRY COPYRIGHT 2005 ACS on STN
RN **81099-88-9** REGISTRY
ED Entered STN: 16 Nov 1984
CN Piperazine, 1-(7-chloro-4-quinolinyl)-4-[(2,4-diamino-6-quinazolinyl)sulfonyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C21 H20 Cl N7 O2 S
LC STN Files: CA, CAPLUS



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

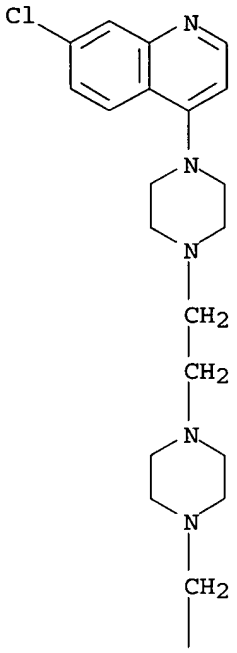
REFERENCE 1: 96:122726

L78 ANSWER 70 OF 86 REGISTRY COPYRIGHT 2005 ACS on STN
RN **53734-41-1** REGISTRY
ED Entered STN: 16 Nov 1984
CN Benzenesulfonamide, 4-amino-N-(5,6-dimethoxy-4-pyrimidinyl)-, mixt. with 5-(4-chlorophenyl)-6-ethyl-2,4-pyrimidinediamine and 4,4'-[1,4-piperazinediylbis(2,1-ethanediyl-4,1-piperazinediyl)]bis[7-chloroquinoline] (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2,4-Pyrimidinediamine, 5-(4-chlorophenyl)-6-ethyl-, mixt. contg. (9CI)
CN Quinoline, 4,4'-[1,4-piperazinediylbis(2,1-ethanediyl-4,1-piperazinediyl)]bis[7-chloro-, mixt. contg. (9CI)
OTHER NAMES:
CN M 1020-fanasil-pyrimethamine mixt.
MF C34 H42 Cl2 N8 . C12 H14 N4 O4 S . C12 H13 Cl N4
CI MXS
LC STN Files: CA, CAPLUS, TOXCENTER

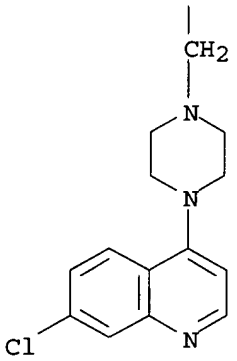
CM 1

CRN 53658-96-1
CMF C34 H42 Cl2 N8

PAGE 1-A

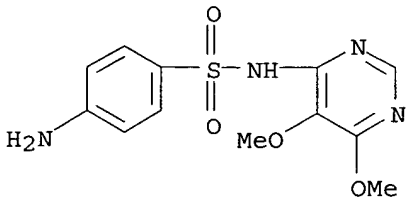


PAGE 2-A



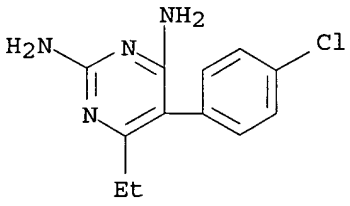
CM 2

CRN 2447-57-6
CMF C12 H14 N4 O4 S



CM 3

CRN 58-14-0
CMF C12 H13 Cl N4



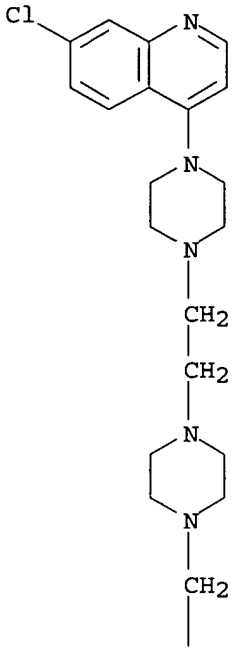
2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 84:99536

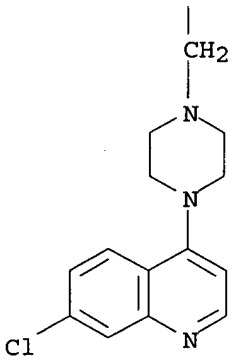
REFERENCE 2: 82:51487

L78 ANSWER 71 OF 86 REGISTRY COPYRIGHT 2005 ACS on STN
RN **53658-96-1** REGISTRY
ED Entered STN: 16 Nov 1984
CN Quinoline, 4,4'-[1,4-piperazinediylbis(2,1-ethanediyl-4,1-piperazinediyl)]bis[7-chloro- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN M 1020
CN Tripiperaquine
FS 3D CONCORD
MF C34 H42 Cl2 N8
CI COM
LC STN Files: BIOSIS, CA, CANCERLIT, CAPLUS, MEDLINE, TOXCENTER

PAGE 1-A



PAGE 2-A



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 143:165983

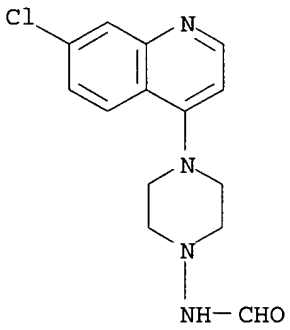
REFERENCE 2: 124:21255

REFERENCE 3: 99:53705

REFERENCE 4: 84:99536

REFERENCE 5: 82:51487

L78 ANSWER 72 OF 86 REGISTRY COPYRIGHT 2005 ACS on STN
RN **32863-66-4** REGISTRY
ED Entered STN: 16 Nov 1984
CN Formamide, N-[4-(7-chloro-4-quinolyl)-1-piperazinyl]- (8CI) (CA INDEX NAME)
FS 3D CONCORD
MF C14 H15 Cl N4 O
LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXCENTER
(*File contains numerically searchable property data)

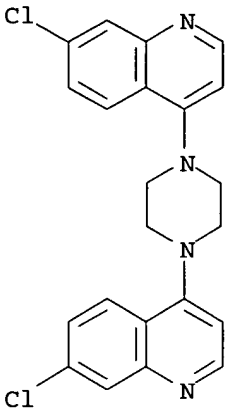


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 75:35658

L78 ANSWER 76 OF 86 REGISTRY COPYRIGHT 2005 ACS on STN
RN **31502-87-1** REGISTRY
ED Entered STN: 16 Nov 1984
CN Quinoline, 4,4'-(1,4-piperazinediyl)bis[7-chloro- (8CI, 9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C22 H18 Cl2 N4
CI COM
LC STN Files: BEILSTEIN*, CA, CAPLUS, CHEMCATS, TOXCENTER
(*File contains numerically searchable property data)



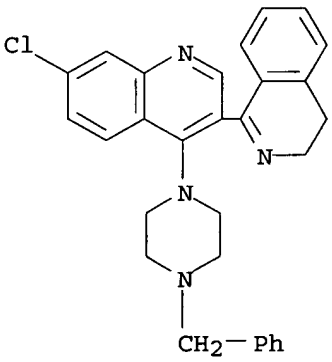
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 105:164484

REFERENCE 2: 74:125372

L78 ANSWER 77 OF 86 REGISTRY COPYRIGHT 2005 ACS on STN
RN **28970-65-2** REGISTRY
ED Entered STN: 16 Nov 1984
CN Quinoline, 4-(4-benzyl-1-piperazinyl)-7-chloro-3-(3,4-dihydro-1-isoquinolyl)-, dihydrochloride (8CI) (CA INDEX NAME)
MF C29 H27 Cl N4 . 2 Cl H
LC STN Files: CA, CAPLUS
CRN (28970-63-0)

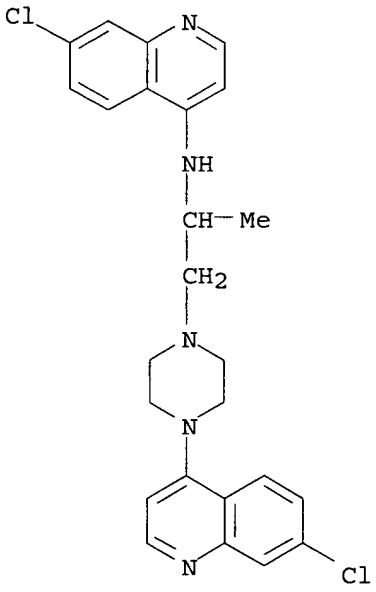


●2 HCl

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 73:55947

L78 ANSWER 82 OF 86 REGISTRY COPYRIGHT 2005 ACS on STN
RN **10547-41-8** REGISTRY
ED Entered STN: 16 Nov 1984
CN Quinoline, 7-chloro-4-[4-[2-[(7-chloro-4-quinolyl)amino]propyl]-1-piperazinyl]- (7CI, 8CI) (CA INDEX NAME)
FS 3D CONCORD
MF C25 H25 Cl2 N5
LC STN Files: CA, CAOLD, CAPLUS



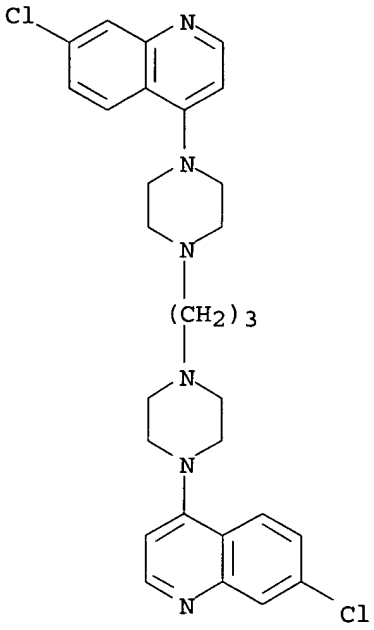
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)
2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 65:31383

L78 ANSWER 83 OF 86 REGISTRY COPYRIGHT 2005 ACS on STN
RN **4085-31-8** REGISTRY
ED Entered STN: 16 Nov 1984
CN Quinoline, 4,4'-(1,3-propanediyldi-4,1-piperazinediyl)bis[7-chloro- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Quinoline, 4,4'-(trimethylenedi-4,1-piperazinediyl)bis[7-chloro- (7CI, 8CI)
OTHER NAMES:
CN Piperaquine
CN Piperaquinoline
FS 3D CONCORD
DR 83764-65-2
MF C29 H32 Cl2 N6

CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, DDFU, DRUGU, EMBASE, IPA, MEDLINE, RTECS*, TOXCENTER
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

27 REFERENCES IN FILE CA (1907 TO DATE)
27 REFERENCES IN FILE CAPLUS (1907 TO DATE)
3 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 143:165983

REFERENCE 2: 143:70972

REFERENCE 3: 142:475029

REFERENCE 4: 142:341958

REFERENCE 5: 141:256909

REFERENCE 6: 141:81712

REFERENCE 7: 140:314381

REFERENCE 8: 140:228324

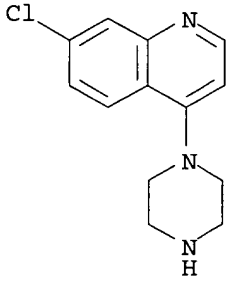
REFERENCE 9: 140:156824

REFERENCE 10: 139:285552

L78 ANSWER 84 OF 86 REGISTRY COPYRIGHT 2005 ACS on STN
RN **900-57-2** REGISTRY
ED Entered STN: 16 Nov 1984
CN Quinoline, 7-chloro-4-(1-piperazinyl)-, (2Z)-2-butenedioate (1:1) (9CI)
(CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Quinoline, 7-chloro-4-(1-piperazinyl)-, (Z)-2-butenedioate (1:1)
CN Quinoline, 7-chloro-4-(1-piperazinyl)-, maleate (7CI)
CN Quinoline, 7-chloro-4-(1-piperazinyl)-, maleate (1:1) (8CI)
FS STEREOSEARCH
MF C13 H14 Cl N3 . C4 H4 O4
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, IFICDB, IFIPAT, IFIUDB
(*File contains numerically searchable property data)

CM 1

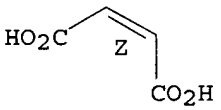
CRN 837-52-5
CMF C13 H14 Cl N3



CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES IN FILE CAPLUS (1907 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

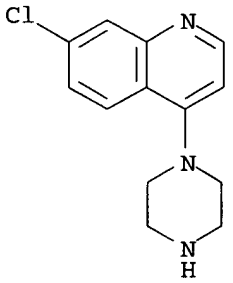
REFERENCE 1: 116:39012

REFERENCE 2: 101:1148

REFERENCE 3: 67:90839

REFERENCE 4: 62:66595

L78 ANSWER 85 OF 86 REGISTRY COPYRIGHT 2005 ACS on STN
RN **837-52-5** REGISTRY
ED Entered STN: 16 Nov 1984
CN Quinoline, 7-chloro-4-(1-piperazinyl)- (7CI, 8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN 4-(1-Piperazinyl)-7-chloroquinoline
CN 7-Chloro-4-(piperazin-1-yl)quinoline
FS 3D CONCORD
MF C13 H14 Cl N3
CI COM
LC STN Files: BEILSTEIN*, BIOSIS, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CSCHEM, IFICDB, IFIPAT, IFIUDB, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

20 REFERENCES IN FILE CA (1907 TO DATE)
20 REFERENCES IN FILE CAPLUS (1907 TO DATE)
2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 143:4019

REFERENCE 2: 140:192195

REFERENCE 3: 140:93938

REFERENCE 4: 140:22645

REFERENCE 5: 136:200479

REFERENCE 6: 134:86277

REFERENCE 7: 129:343400

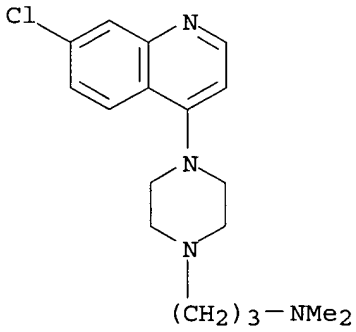
REFERENCE 8: 128:257447

REFERENCE 9: 128:48119

REFERENCE 10: 122:160450

L78 ANSWER 86 OF 86 REGISTRY COPYRIGHT 2005 ACS on STN
RN **298-78-2** REGISTRY
ED Entered STN: 16 Nov 1984
CN 1-Piperazinepropanamine, 4-(7-chloro-4-quinolinyl)-N,N-dimethyl- (9CI) (CA INDEX NAME)

```
OTHER CA INDEX NAMES:
CN   Quinoline, 7-chloro-4-[4-[3-(dimethylamino)propyl]-1-piperazinyl]- (7CI,
     8CI)
OTHER NAMES:
CN   7-Chloro-4-[4-[3-(dimethylamino)propyl]-1-piperazinyl]quinoline
FS   3D CONCORD
MF   C18 H25 Cl N4
CI   COM
LC   STN Files:   BEILSTEIN*, CA, CAOLD, CAPLUS
         (*File contains numerically searchable property data)
```




```
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

               2 REFERENCES IN FILE CA (1907 TO DATE)
               2 REFERENCES IN FILE CAPLUS (1907 TO DATE)
               2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE   1:  62:69264

REFERENCE   2:  62:66595


=> □

=> d stat que l80 nos
L66             STR
L68         601 SEA FILE=REGISTRY SSS FUL L66
L69             STR
L70          12 SEA FILE=REGISTRY SUB=L68 SSS FUL L69
L71           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L70
L72         589 SEA FILE=REGISTRY ABB=ON  PLU=ON  L68 NOT L70
L73         102 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L72
L74          86 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L73 AND PD=<OCTOBER 24, 2003
L75          86 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L74 NOT L71
L76          20 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L75 AND PATENT/DT
L77          66 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L75 NOT L76
L79          19 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("DUNNING L"/AU OR "DUNNING L
                A"/AU OR "DUNNING L K"/AU OR "DUNNING L KAY"/AU OR "DUNNING L
                L"/AU OR "DUNNING L M"/AU OR "DUNNING LAURA"/AU)
L80          18 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L79 NOT (L71 OR L76 OR L77)


=>
=>
```

=> d ibib abs l80 1-18

L80 ANSWER 1 OF 18 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:129178 HCAPLUS
TITLE: Structure Function Differences in Nonpeptide CCR1 Antagonists for Human and Mouse CCR1
AUTHOR(S): Onuffer, James; McCarrick, Margaret A.; **Dunning, Laura**; Liang, Meina; Rosser, Mary; Wei, Guo-Ping; Ng, Howard; Horuk, Richard
CORPORATE SOURCE: Department of Immunology, Berlex Biosciences, Richmond, CA, 94806, USA
SOURCE: Journal of Immunology (2003), 170(4), 1910-1916
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A useful strategy for identifying ligand binding domains of G protein-coupled receptors has been the exploitation of species differences in antagonist potencies. We have used this approach for the CCR1 chemokine receptor with a novel series of antagonists, the 4-hydroxypiperidines, which were discovered by high throughput screening of human CCR1 and subsequently optimized. The structure-activity relationships for a number of different 4-hydroxypiperidine antagonists for human and mouse CCR1 were examined by receptor binding and functional assays. These compds. exhibit major differences in their rank order of potency for the human and mouse chemokine receptor CCR1. For example, the initial lead template, BX 510, which was a highly potent functional antagonist for human CCR1 (Ki = 21 nM) was >400-fold less active on mouse CCR1 (Ki = 9150 nM). However, increasing the length of the linker between the piperidine and dibenzothiepine groups by one methylene group generated a compound, BX 511, which was equipotent for both human and mouse CCR1. These and other analogs of the lead template BX 510, which have major differences in potency for human and mouse CCR1, are described, and a model for their interaction with human CCR1 is presented.
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 2 OF 18 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:618185 HCAPLUS
TITLE: Synthesis and SAR of CCR1-specific nonpeptide antagonists
AUTHOR(S): Islam, Imadul; May, Karen; Bauman, John; Ghannam, Ameen; Ng, Howard P.; Monahan, Sean; Wei, Guo-Ping; Xu, Wei; Liang, Meina; **Dunning, Laura**; Subramanyam, Babu; Shen, Jun; Walters, Janette; Ho, Elena; Horuk, Richard
CORPORATE SOURCE: Berlex Biosciences, Richmond, CA, 94804, USA
SOURCE: Abstracts of Papers, 224th ACS National Meeting, Boston, MA, United States, August 18-22, 2002 (2002), MEDI-334. American Chemical Society: Washington, D. C.
CODEN: 69CZPZ
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB There is overwhelming evidence in support of the concept that the CC chemokines macrophage inflammatory protein-1α (MIP-1α) and RANTES play an important role in the pathogenesis of chronic inflammatory diseases. Since MIP-1α and RANTES are ligands for the CCR1 chemokine receptor, we developed an assay to identify antagonists for this

receptor as a novel therapeutic approach for treating patients with certain inflammatory disorders. Through high capacity screening, followed by chemical optimization, we identified a novel series of piperazine-containing CCR-1 antagonists. The synthesis, structure-activity relationships and biol. data of potent and selective CCR-1 antagonists will be described.

L80 ANSWER 3 OF 18 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:259748 HCAPLUS
DOCUMENT NUMBER: 135:132021
TITLE: CCR1-specific non-peptide antagonist: efficacy in a rabbit allograft rejection model
AUTHOR(S): Horuk, R.; Shurey, S.; Ng, H. P.; May, K.; Bauman, J. G.; Islam, I.; Ghannam, A.; Buckman, B.; Wei, G. P.; Xu, W.; Liang, M.; Rosser, M.; **Dunning, L.**; Hesselgesser, J.; Snider, R. M.; Morrissey, M. M.; Perez, H. D.; Green, C.
CORPORATE SOURCE: Department of Immunology, Berlex Biosciences, Richmond, CA, 94806, USA
SOURCE: Immunology Letters (2001), 76(3), 193-201
CODEN: IMLED6; ISSN: 0165-2478
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The classic signs of acute cellular rejection during organ transplantation include the infiltration of mononuclear cells into the interstitium. This recruitment of leukocytes into the transplanted tissue is promoted by chemokines like RANTES. Since RANTES is a potent agonist for the CC chemokine receptor CCR1, the authors examined whether the CCR1 antagonist BX 471 was efficacious in a rabbit kidney transplant rejection model. BX 471 was able to compete with high affinity with the CCR1 ligands MIP-1α and RANTES for binding to HEK 293 cells expressing rabbit CCR1. BX 471 was a competitive antagonist of rabbit CCR1 in Ca2+ flux studies. Two sep. studies in which animals were s.c. implanted with slow release pellets of BX 471 demonstrated that animals implanted with BX 471 had increased survival compared with untreated controls or animals implanted with placebo. The mean survival time for the placebo group was 12.33 days. The animals in the BX 471 treated group had mean survival times of 16.9 and 16.0 days, resp., for the two studies. Anal. of the combined data by Student t-test gave a P value of 0.03 that is significant at the 0.05 level. In addition, there was a marked reduction in the urea and creatinine
levels in the BX 471 treated animals compared with the control and placebo groups in both studies. Finally, pathol. anal. of the kidneys in the rabbit renal transplantation model from animals in the different groups showed that BX 471 was similar to cyclosporin in its ability to prevent extensive infarction of transplanted kidneys. Based on the data from these studies, BX 471 shows clear efficacy at the single dose tested compared with animals treated with placebo.
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 4 OF 18 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:125409 HCAPLUS
DOCUMENT NUMBER: 134:279391
TITLE: A non-peptide functional antagonist of the CCR1 chemokine receptor is effective in rat heart transplant rejection
AUTHOR(S): Horuk, Richard; Clayberger, Carol; Krensky, Alan M.; Wang, Zhaohui; Grone, Hermann-Josef; Weber, Christian; Weber, Kim S. C.; Nelson, Peter J.; May, Karen;

Rosser, Mary; **Dunning, Laura**; Liang, Meina; Buckman, Brad; Ghannam, Ameen; Ng, Howard P.; Islam, Imadul; Bauman, John G.; Wei, Guo-Ping; Monahan, Sean; Xu, Wei; Snider, R. Michael; Morrissey, Michael M.; Hesselgesser, Joseph; Perez, H. Daniel

CORPORATE SOURCE: Department of Immunology, Berlex Biosciences, Richmond, CA, 94806, USA

SOURCE: Journal of Biological Chemistry (2001), 276(6), 4199-4204
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Chemokines like RANTES appear to play a role in organ transplant rejection. Because RANTES is a potent agonist for the chemokine receptor CCR1, we examined whether the CCR1 receptor antagonist BX471 is efficacious in a rat heterotopic heart transplant rejection model. Treatment of animals with BX471 and a subtherapeutic dose of cyclosporin (2.5 mg/kg), which is by itself ineffective in prolonging transplant rejection, is much more efficacious in prolonging transplantation rejection than animals treated with either cyclosporin or BX471 alone. We have examined the mechanism of action of the CCR1 antagonist in in vitro flow assays over microvascular endothelium and have discovered that the antagonist blocks the firm adhesion of monocytes triggered by RANTES on inflamed endothelium. Together, these data demonstrate a significant role for CCR1 in allograft rejection.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 5 OF 18 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:445772 HCAPLUS

DOCUMENT NUMBER: 133:171945

TITLE: Identification and characterization of potent, selective, and orally active antagonist of the CC chemokine receptor-1

AUTHOR(S): Liang, Meina; Mallari, Cornell; Rosser, Mary; Ng, Howard P.; May, Karen; Monahan, Sean; Bauman, John G.; Islam, Imadul; Ghannam, Ameen; Buckman, Brad; Shaw, Ken; Wei, Guo-Ping; Xu, Wei; Zhao, Zuchun; Ho, Elena; Shen, Jun; Oanh, Huynh; Subramanyam, Babu; Vergona, Ron; Taub, Dennis; **Dunning, Laura**; Harvey, Susan; Snider, R. Michael; Hesselgesser, Joseph; Morrissey, Michael M.; Perez, H. Daniel; Horuk, Richard

CORPORATE SOURCE: Department of Discovery Research, Berlex Biosciences, Richmond, CA, 94804, USA

SOURCE: Journal of Biological Chemistry (2000), 275(25), 19000-19008
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The CC chemokine receptor-1 (CCR1) is a prime therapeutic target for treating autoimmune diseases. Through high capacity screening followed by chemical optimization, we identified a novel non-peptide CCR1 antagonist, R-N-[5-chloro-2-[2-[4-[(4-fluorophenyl)methyl]-2-methyl-1-pipera zinyl]-2-oxoethoxy]phenyl]urea hydrochloric acid salt (BX 471). Competition binding studies revealed that BX 471 was able to displace the

CCR1 ligand macrophage inflammatory protein-1α (MIP-1α), RANTES, and monocyte chemotactic protein-3 (MCP-3) with high affinity (Ki ranged from 1 nM to 5.5 nM). BX 471 was a potent functional antagonist based on its ability to inhibit a number of CCR1-mediated effects including Ca2+ mobilization, increase in extracellular acidification rate, CD11b expression, and leukocyte migration. BX 471 demonstrated a greater than 10,000-fold selectivity for CCR1 compared with 28 G-protein-coupled receptors. Pharmacokinetic studies demonstrated that BX 471 was orally active with a bioavailability of 60% in dogs. Furthermore, BX 471 effectively reduces disease in a rat exptl. allergic encephalomyelitis model of multiple sclerosis. This study is the first to demonstrate that a non-peptide chemokine receptor antagonist is efficacious in an animal model of an autoimmune disease. In summary, we have identified a potent, selective, and orally available CCR1 antagonist that may be useful in the treatment of chronic inflammatory diseases.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 6 OF 18 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:127362 HCAPLUS
DOCUMENT NUMBER: 132:303163
TITLE: Species selectivity of a small molecule antagonist for the CCR1 chemokine receptor
AUTHOR(S): Liang, M.; Rosser, M.; Ng, H. P.; May, K.; Bauman, J. G.; Islam, I.; Ghannam, A.; Kretschmer, P. J.; Pu, H.; **Dunning, L.**; Snider, R. M.; Morrissey, M. M.; Hesselgesser, J.; Perez, H. D.; Horuk, R.
CORPORATE SOURCE: Department of Pharmaceuticals Discovery, Berlex Biosciences, Richmond, CA, USA
SOURCE: European Journal of Pharmacology (2000), 389(1), 41-49
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The species specificity of a small mol. antagonist for the human CCR1 chemokine receptor, (2,2-diphenyl-5-(4-chlorophenyl)4-hydroxypiperidin-1-yl) valeronitrile (CCR1 antagonist 1), has been examined using cloned CCR1 receptors from various species. The compound was able to bind to rabbit, marmoset, and human CCR1, and was able to block the functional activation of these receptors. However, it failed to significantly displace radiolabeled macrophage inflammatory protein-1α (MIP-1α) binding to mouse CCR1 at concns. up to 10 μM. These data suggested that the antagonist binding site is well-conserved in rabbit, marmoset and human CCR1, but not in mouse CCR1. The functional selectivity and mechanism of action for CCR1 antagonist 1 were further characterized. CCR1 antagonist 1 blocked the increase in intracellular Ca2+ stimulated by CCR1 agonists, but had no effect on N-formyl-Met-Leu-Phe (FMLP), monocyte chemotactic protein-1 (MCP-1) and stromal-derived factor 1α (SDF1α)-induced Ca2+ mobilization, demonstrating functional selectivity for CCR1. Since CCR1 antagonist 1 is a functional antagonist of marmoset and rabbit CCR1 receptors, it should be possible to test its efficacy in animal models of disease.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

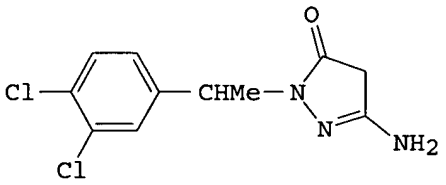
L80 ANSWER 7 OF 18 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:704352 HCAPLUS
DOCUMENT NUMBER: 132:45141
TITLE: Within-person variability of the ratios of urinary 2-hydroxyestrone to 16α-hydroxyestrone in

Caucasian women
AUTHOR(S): Chen, Z.; Zheng, W.; **Dunning, L. M.**; Anderson, K. G.; Parrish, R. S.; Holtzman, J. L.
CORPORATE SOURCE: Molecular Epidemiology Unit, University of South Carolina School of Public Health, South Carolina Cancer Center, Columbia, SC, USA
SOURCE: Steroids (1999), 64(12), 856-859
CODEN: STEDAM; ISSN: 0039-128X
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The ratio of urinary 2-hydroxyestrone (2-OHE1) to 16α-hydroxyestrone (16α-OHE1) has been suggested as a potential biomarker for breast cancer risk. The authors evaluated within-person variability of this biomarker in ten healthy Caucasian women aged 23-58 yr. Each study participant was asked to provide an overnight fasting morning urine sample once a week for an average of 8 wk. These urine samples were assayed for 2-OHE1 and 16α-OHE1 by using competitive enzyme immunoassay kits purchased from the ImmunaCare Corporation. The coeffs. of variation for urinary 2-OHE1/16α-OHE1 over the study period ranged from 13.7 to 59.6% (mean, 33.3%) in the authors' study participants. There was a good correlation between the level of the urinary 2-OHE1/16α-OHE1 ratio in any single urine sample and the average ratio over the 8-wk study period from the same woman, with the mean correlation coefficient of 0.85. These results indicated that the within-person variation of the 2-OHE1 to 16α-OHE1 ratio for most women was moderate and the level of this ratio in a single urine sample, in general, reflects reasonably well the level of this biomarker over a 2-mo period.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 8 OF 18 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:91093 HCAPLUS
DOCUMENT NUMBER: 112:91093
TITLE: Determination of muzolimine in plasma and urine by high-performance liquid chromatography
AUTHOR(S): Osman, M. A.; **Dunning, L. K.**; Bhavnagri, V. P.; Cheng, L. K.
CORPORATE SOURCE: Drug Metab. Dep., A. H. Robins Co., Richmond, VA, 23220, USA
SOURCE: Journal of Chromatography (1989), 496(2), 478-84
CODEN: JOCRAM; ISSN: 0021-9673
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

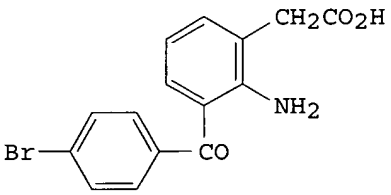


I

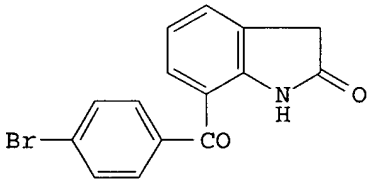
AB A sensitive and selective HPLC method for the determination of muzolimine(I) in plasma and urine was based on the use of a C18 reversed-phase (RP) μBondapak column for plasma and a RP Ph Nova Pak column for urine. The

mobile phase for plasma was MeCN-0.05M phosphate butter pH 4.2 (45:55) and the same system (28:72) for urine with detection at 272 nm. The concentration-response curve was linear over 0-10 μg/mL. The method has a high degree of precision and accuracy. The method was used for both animal and human bioavailability studies.

L80 ANSWER 9 OF 18 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1989:224881 HCAPLUS
DOCUMENT NUMBER: 110:224881
TITLE: Determination of bromfenac in plasma by high-performance liquid chromatography
AUTHOR(S): Osman, M. A.; **Dunning, L. K.**; Cheng, L. K.; Wright, G. J.
CORPORATE SOURCE: Drug Metab. Dep., A. H. Robins Co., Richmond, VA, 23220, USA
SOURCE: Journal of Chromatography (1989), 489(2), 452-8
CODEN: JOCRAM; ISSN: 0021-9673
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 110:224881
GI



I



II

AB A sensitive and selective HPLC method using a reversed-phase μBondapak C18 column, 0.05M NaOAc buffer (pH 6.5)-MeCN-THF (55:39:6) mobile phase and UV detection at 270 nm was developed for determination of bromfenac (I) in plasma. The method had a linear range from 0.03-1.0 μg/mL when 0.5 mL plasma was used. The method showed good precision and accuracy. An extraction scheme was used based on extracting the cyclic form (II) of I present in blood. First in alkaline medium and then converting the remaining I to II in acidic medium. II is readily extractable into organic solvents.

L80 ANSWER 10 OF 18 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:15830 HCAPLUS
DOCUMENT NUMBER: 108:15830
TITLE: Efficacy of levamisole/famphur paste for control of cattle grubs (Diptera: Oestridae) and gastrointestinal worms (Nematoda: Trichostrongylidae)
AUTHOR(S): Campbell, J. B.; Knapp, F. W.; Loomis, E. C.; Boxler, D. J.; Herald, F.; **Dunning, L. L.**
CORPORATE SOURCE: West Cent. Res. Cent., Univ. Nebraska, North Platte, NE, 69101, USA
SOURCE: Journal of Economic Entomology (1987), 80(5), 1028-30
CODEN: JEENAI; ISSN: 0022-0493
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Research trials in California, Nebraska, and Kentucky have shown that an exptl. paste containing levamisole at a constant rate and famphur at several rates will control both cattle grubs, Hypoderma lineatum and H. bovis, and gastrointestinal worms. A paste containing 11.5% levamisole (8 mg/kg) and

21.6% famphur (30 mg/kg) provided grub control equivalent to that of either famphur or ivermectin and gastrointestinal worm control comparable with that of levamisole or ivermectin.

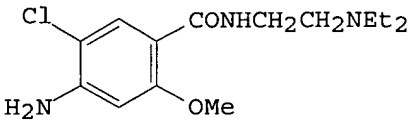
L80 ANSWER 11 OF 18 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1984:63476 HCAPLUS
DOCUMENT NUMBER: 100:63476
TITLE: Effectiveness of Ectiban, egg oil, Rabon, or Sevin for control of northern fowl mites on laying hens
AUTHOR(S): McKeen, W. D.; Loomis, E. C.; **Dunning, L. L.**
CORPORATE SOURCE: Agric. Coop. Exten., Univ. California, San Bernardino, CA, 92415, USA
SOURCE: Poultry Science (1983), 62(12), 2343-6
CODEN: POSCAL; ISSN: 0032-5791
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two field trials were conducted to control northern fowl mite (Ornithonyssus sylviarum) on White Leghorn hens. Ectiban [52645-53-1] spray and dust treatments were compared to Rabon [22248-79-9] and Sevin [63-25-2] spray-treatments. Egg oil, Rabon, and Sevin sprays were tested in another trial. Concentration and rates of application followed label recommendations. Ectiban spray gave excellent control; Ectiban dust, Rabon, and Sevin spray treatments resulted in poor control. The failure of Sevin suggests the possibility of resistance.

L80 ANSWER 12 OF 18 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1980:111795 HCAPLUS
DOCUMENT NUMBER: 92:111795
TITLE: GR nylon-6 (STX sheet) stamping
AUTHOR(S): **Dunning, L. A.**; Ward, L. G.
CORPORATE SOURCE: Fibers Div., Allied Chem. Corp., Morristown, NJ, 07960, USA
SOURCE: More Plast. Growth, Answer Transp. 80's, Natl. Tech. Conf., Soc. Plast. Eng. (1979), 41-3. SPE: Greenwich, Conn.
CODEN: 42IGAO
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Long-term experiences in the production of glass fiber-reinforced nylon 6 [25038-54-4] sheets by hot-stamping using steel stamping presses and hydraulic presses for compression molding are summarized and methods providing fast consistent production cycles for manufacture of automotive parts are discussed.

L80 ANSWER 13 OF 18 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1980:53342 HCAPLUS
DOCUMENT NUMBER: 92:53342
TITLE: Comparative effectiveness of fenvalerate and carbaryl sprays against the northern fowl mite
AUTHOR(S): Loomis, E. C.; Bramhall, E. L.; **Dunning, L. L.**
CORPORATE SOURCE: Vet. Ext., Univ. California, Davis, CA, 95616, USA
SOURCE: Journal of Economic Entomology (1979), 72(6), 856-9
CODEN: JEENAI; ISSN: 0022-0493
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In 2 field tests on a poultry ranch, different concns. of fenvalerate [51630-58-1], were compared against the standard carbaryl [63-25-2] by hand and power sprays to layer hens for control of Ornithonyssus sylviarum. Experiment hand spray concns. of 0.05 and 0.025% fenvalerate and 0.5% carbaryl

produced effective mite control for 2 mo during which time the treated hens were challenged with mites at 3, 6, and 8 wk posttreatment. In a 2nd test, com. power sprays of 0.025 and 0.0125% fenvalerate produced effective mite control for 53 days. No adverse effects, loss in egg prodn, or abnormal mortality occurred in hens sprayed with fenvalerate.

L80 ANSWER 14 OF 18 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1978:98863 HCAPLUS
DOCUMENT NUMBER: 88:98863
TITLE: Metoclopramide metabolism and determination by high-pressure liquid chromatography
AUTHOR(S): Teng, Lina; Bruce, Robert B.; **Dunning, L. Kay**
CORPORATE SOURCE: A. H. Robins Res. Lab., Richmond, VA, USA
SOURCE: Journal of Pharmaceutical Sciences (1977), 66(11), 1615-18
CODEN: JPMSAE; ISSN: 0022-3549
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB A high-pressure liquid chromatog. method suitable for determining plasma metoclopramide (I) [364-62-5] levels at therapeutic (10-20 mg) doses is described. Eight metabolites as well as I were isolated and identified in rat, dog, and human urine. The only common metabolite in these species is 2-[4-amino-5-chloro-2-methoxybenzoyl)amino]acetic acid. [65567-29-5]. N-Deethylation is a major pathway for I metabolism in the lower animals but not in humans. I is excreted mainly unchanged or as its conjugates by humans.

L80 ANSWER 15 OF 18 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1973:428345 HCAPLUS
DOCUMENT NUMBER: 79:28345
TITLE: Control of Hypoderma lineatum and H. bovis in California, 1970-72, using crufomate, fenthion, and imidan in new low-volume and usual pour-on formulations
AUTHOR(S): Loomis, E. C.; **Dunning, L. L.**; Riehl, L. A.
CORPORATE SOURCE: Univ. California, Davis, CA, USA
SOURCE: Journal of Economic Entomology (1973), 66(2), 439-43
CODEN: JEENAI; ISSN: 0022-0493
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cattle grub (H. bovis and H. lineatum) reduction in 14 herds following low volume and pour-on applications of fenthion (I) [55-38-9] were 96.4 and 95.6%, resp., while that for crufomate (II) [299-86-5] applications was 91 and 100%, resp. Average grub reduction for pour-on applications, alone, were 98.6% for Imidan (III) [732-11-6] and 93.6% for fenthion in 6 herds. No adverse side effects were observed in any cattle treated with the various systemics.

L80 ANSWER 16 OF 18 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1972:415565 HCAPLUS

DOCUMENT NUMBER: 77:15565
TITLE: Systemic insecticide study on livestock in California, 1967-68. 2. Evaluation of Imidan for cattle grub control
AUTHOR(S): Loomis, E. C.; Crenshaw, G. L.; **Dunning, L. L.**
CORPORATE SOURCE: Agric. Ext. Serv., Univ. California, Davis, CA, USA
SOURCE: Journal of Economic Entomology (1972), 65(2), 450-3
CODEN: JEENAI; ISSN: 0022-0493
DOCUMENT TYPE: Journal
LANGUAGE: English
AB By pour-on application, cattle grub was totally controlled using 26 mg Imidan (I) [732-11-6]/kg, and almost totally controlled using 7.5 mg fenthion [55-38-9]/kg and 25 mg trichlorfon [52-68-6]/kg. Spray applications were effective only early in the season. Mild side effects were shown by some Imidan-treated calves, especially when applied late in the season. The species were mostly the common cattle grub Hypoderma lineatum, and to a lesser extent the northern cattle grub H. bovis.

L80 ANSWER 17 OF 18 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1970:497804 HCAPLUS
DOCUMENT NUMBER: 73:97804
TITLE: Systemic insecticide study on livestock in california, 1965-67. 1. Cattle grub control
AUTHOR(S): Loomis, E. C.; Crenshaw, G. L.; Bushnell, R. B.; **Dunning, L. L.**
CORPORATE SOURCE: Agr. Ext. Serv., Univ. of California, Davis, CA, USA
SOURCE: Journal of Economic Entomology (1970), 63(4), 1237-41
CODEN: JEENAI; ISSN: 0022-0493
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Comparative evaluation data for grub control are presented on 5 animal systemic insecticides: coumaphos, crufomate, Imidan, fenthion, and trichlorfom. Grub reduction averaged 95% with the 2 crufomate formulations (25% effective concentration (EC) as a pour-on at 1:2 or 1:3 dilution or as a 0.25% spray) and 8R (9.6% pour-on), and trichlorfon (8% pour-on). Coumaphos showed from poor (0%) to good (98%) results dependent on time and method of application, while Imidan was more effective as a pour-on (100%) than as a spray (average 80%) and when used early (average 80%) rather than late (average 32%) in the grub-control season. The 2.5% pour-on formulation of fenthion averaged 46% grub reduction from 2 herds treated. Nearly all spray applications were made at half gallon per head, which is half the usual amount applied by other investigators and far less than the amount resulting from com. recommendations of wetting the skin or hair coat of the entire animal. Following spray recommendations excessive run-off and unnecessary waste of material was observed particularly with calves and yearlings or for mature cattle with short hair coats. Hypoderma lineatum was predominant over H. bovis in northern herds, while H. bovis was absent in southern herds. Special H. bovis surveys made during 1966 and 1967 in southern California showed that this species was found mainly in yearlings, 1st calf heifers, and cows imported from northern California and out of state. The fact that H. bovis does not occur commonly in this region may be due to changes from 1947 to 1967 in origin of cattle in beef feedlot operations and in drylot management of dairy cows.

L80 ANSWER 18 OF 18 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1965:80965 HCAPLUS
DOCUMENT NUMBER: 62:80965
ORIGINAL REFERENCE NO.: 62:14305e-f

TITLE: Use photomicrographs for fast P. E. analysis
AUTHOR(S): **Dunning, L. M.**; Ilkanic, T. J.
CORPORATE SOURCE: Ferro Corp., Cleveland, OH
SOURCE: Ceram. Ind. (1965), 84(2), 36-8
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Photomicrographs of sections of porcelain enamel frit are recorded on a Polaroid Land camera. By this means laminations, blisters, fishscale, and other defects can be observed and recorded for comparison. A magnification of 60X is recommended.

=> => d stat que l82 nos
L66 STR
L68 601 SEA FILE=REGISTRY SSS FUL L66
L69 STR
L70 12 SEA FILE=REGISTRY SUB=L68 SSS FUL L69
L71 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L70
L72 589 SEA FILE=REGISTRY ABB=ON PLU=ON L68 NOT L70
L73 102 SEA FILE=HCAPLUS ABB=ON PLU=ON L72
L74 86 SEA FILE=HCAPLUS ABB=ON PLU=ON L73 AND PD=<OCTOBER 24, 2003
L75 86 SEA FILE=HCAPLUS ABB=ON PLU=ON L74 NOT L71
L76 20 SEA FILE=HCAPLUS ABB=ON PLU=ON L75 AND PATENT/DT
L77 66 SEA FILE=HCAPLUS ABB=ON PLU=ON L75 NOT L76
L79 19 SEA FILE=HCAPLUS ABB=ON PLU=ON ("DUNNING L"/AU OR "DUNNING L A"/AU OR "DUNNING L K"/AU OR "DUNNING L KAY"/AU OR "DUNNING L L"/AU OR "DUNNING L M"/AU OR "DUNNING LAURA"/AU)
L80 18 SEA FILE=HCAPLUS ABB=ON PLU=ON L79 NOT (L71 OR L76 OR L77)
L81 38 SEA FILE=HCAPLUS ABB=ON PLU=ON ("JAROCH S"/AU OR "JAROCH STEFAN"/AU)
L82 37 SEA FILE=HCAPLUS ABB=ON PLU=ON L81 NOT (L71 OR L76 OR L77 OR L80)

=>
=>

=> d ibib abs l82 1-37

L82 ANSWER 1 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:863973 HCAPLUS
TITLE: Putting small molecules in the lead
AUTHOR(S): **Jaroch, Stefan**; Weinmann, Hilmar
CORPORATE SOURCE: Research Center Europe, Medicinal Chemistry, Schering AG, Berlin, D-13342, Germany
SOURCE: Nature Chemical Biology (2005), 1(4), 180-183
CODEN: NCBABT; ISSN: 1552-4450
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Chemical genomic approaches offer an alternative to traditional high-throughput screening for drug discovery and provide an emerging approach to probing cellular biol. The 58th Ernst Schering Foundation Workshop on "Cheical Genomics: Small Mol. Probes to Study Cellular Function," held Apr. 6-8, 2005, in Berlin, Germany, captured recent chemical genomics advances and highlighted the power of a tight integration of chemical and biol.

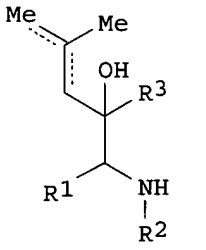
L82 ANSWER 2 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:347003 HCAPLUS

DOCUMENT NUMBER: 142:410957
TITLE: Preparation of 4-methyl-4-penten-1-amines and related compounds as antiphlogistics
INVENTOR(S): Rehwinkel, Hartmut; Baeurle, Stefan; Berger, Markus; Schmees, Norbert; Schaecke, Heike; Krolikiewicz, Konrad; Mengel, Anne; Nguyen, Duy; **Jaroch, Stefan**; Skuballa, Werner
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

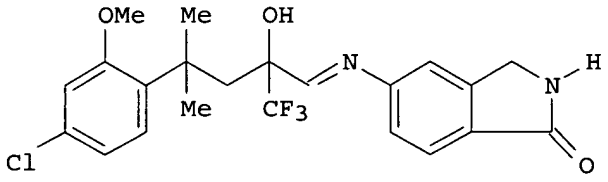
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005035518	A1	20050421	WO 2004-EP11375	20041006
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10347385	A1	20050512	DE 2003-10347385	20031008
US 2005131226	A1	20050616	US 2004-960757	20041008

PRIORITY APPLN. INFO.:
DE 2003-10347385 A 20031008
US 2003-511576P P 20031016

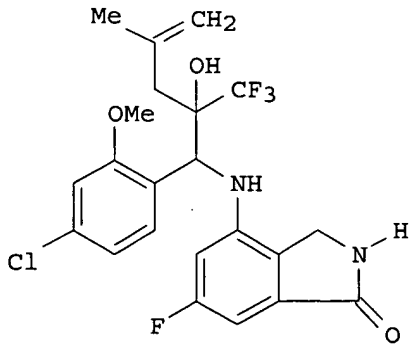
GI



I



II



III

AB Title compds. I [R1 = (un)substituted phenyl; R2 = mono or bicyclic aromatic with provisos] and their pharmaceutically acceptable salts were prepared For example, BBr3 meditated aza-claisen rearrangement imine II, e.g., prepared from 5-fluoro-2-methylbenzoic acid in 8-steps, afforded aminopentanol III in 17% yield. Compds. I are claimed to be useful as antiphlogistics.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 3 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:346991 HCAPLUS

DOCUMENT NUMBER: 142:411246

TITLE: Method for the production of 1-(quinoline amino)- and 1-(isoquinoline amino)-substituted pentan-2-ols and their use as anti-inflammatories

INVENTOR(S): **Jaroch, Stefan**; Baeurle, Stefan; Berger, Markus; Krolikiewicz, Konrad; Nguyen, Duy; Rehwinkel, Hartmut; Schmees, Norbert; Skuballa, Werner; Schaecke, Heike

PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany

SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

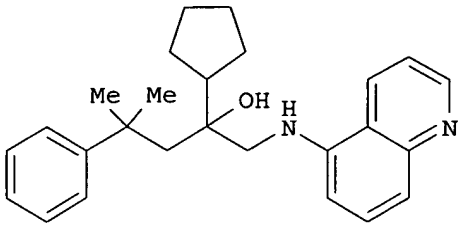
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005035502	A1	20050421	WO 2004-EP10880	20040924
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10346940	B3	20050616	DE 2003-10346940	20031006
US 2005143415	A1	20050630	US 2004-957742	20041005

PRIORITY APPLN. INFO.:

DE 2003-10346940	A	20031006
DE 2000-10038639	A	20000728
US 2003-510091P	P	20031010

OTHER SOURCE(S): MARPAT 142:411246

GI



I

AB The invention relates to substituted pentanols, ACR1R2CH2CR3(OH)BNHQ [A = aryl, CH2Ph, CH2CH2Ph {optionally substituted with C1-5-alkyl, C1-5-alkoxy, C1-5-alkylthio, C1-5-perfluoroalkyl, halogen, OH, CN, NO2, O(CH2)nO, O(CH2)nCH2, OCH:CH, (CH2)n+2, NR4R5; n = 1, 2}; R1, R2 = H, Me, Et; CR1R2 = C3-6-cycloalkyl; R3 = C4-8-alkyl, C2-6-alkenyl, C2-6-alkynyl, C3-8-cycloalkyl, C3-7-heterocyclyl, aryl, heteroaryl, (C1-8-alkyl)-(C3-8-cycloalkyl), (C1-8-alkyl)-aryl, (C1-8-alkyl)-heteroaryl; B = CH2, CHMe, CHEt, C(:O); Q = quinolinyl, isoquinolinyl, (optionally substituted with C1-5-alkyl, C1-5-alkoxy, C1-5-alkylthio, C1-5-perfluoroalkyl, halogen, OH, CN, NO2, NR4R5); R4, R5 = H, C1-5-alkyl, CO-(C1-5-alkyl)], their racemates, stereoisomers and physiol. acceptable salts, to a method for their production and to their use as anti-inflammatories (no data). Thus, cyclopentylpentanol I was prepared from PhCMe2OH via reaction with Me3SiOCH:CHCO2Et in CH2Cl2 containing ZnCl4, Grignard reaction in THF with cyclopentylmagnesium chloride in Et2O, LiAlH4 reduction, oxidn, with pyridine.SO3 complex in DMSO, amination with 5-aminoquinoline in MeCO2H containing NaBO(OAc)3 followed by reduction with NaBH4 in THF.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 4 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:346851 HCAPLUS
DOCUMENT NUMBER: 142:430128
TITLE: Preparation of 1-(hetero)arylamino-1,2,3,4-tetrahydronaphthalenes as antiinflammatories.
INVENTOR(S): Rehwinkel, Hartmut; Baeurle, Stefan; Berger, Markus; Schmees, Norbert; Schaecke, Heike; Krolikiewicz, Konrad; Mengel, Anne; Nguyen, Duy; **Jaroch, Stefan**; Skuballa, Werner
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 292 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005034939	A1	20050421	WO 2004-EP11370	20041006

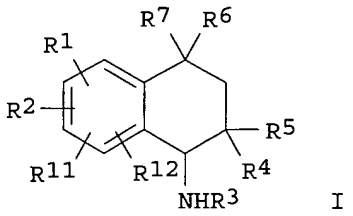
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE 10347386	A1	20050519	DE 2003-10347386	20031008
DE 10347383	A1	20050525	DE 2003-10347383	20031008
US 2005171109	A1	20050804	US 2004-962169	20041012
PRIORITY APPLN. INFO.:			DE 2003-10347383 A	20031008
			DE 2003-10347386 A	20031008
			DE 2004-102004017662A	20040405
			US 2003-510152P P	20031014

OTHER SOURCE(S): MARPAT 142:430128

GI



I

AB Title compds. [I; R1, R2 = H, OH, halo, (substituted) alkyl, alkoxy, alkylthio, perfluoroalkyl, cyano, NO2; R1R2 = O(CH2)nO, O(CH2)nCH2, OCH:CH, etc.; n = 1, 2; R11 = H, OH, halo, cyano, (substituted) alkyl, alkoxy, alkylthio, perfluoroalkyl; R12 = H, OH, halo, cyano, (substituted) alkyl, alkoxy; R3 = (substituted) alkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, etc.; R4 = OH, OR10, O2CR10; R10 = protecting group, alkyl; R5 = (fluorinated) alkyl, cycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, heterocyclyl, aryl, alkylaryl, heteroaryl, etc.; R6, R7 = H, Me, Et; R6R7C = atoms to form a cycloalkyl ring], were prepared for treatment of inflammation (no data). Thus, 4-(5-fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentanal (preparation given) and 4-amino-2,3-dihydroisoindol-1-one (preparation given) were stirred 4 days in HOAc to give 75.5% 4-[[4-(5-fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-(trifluoromethyl)pentyliden]amino]-2,3-dihydroisoindol-1-one. The latter was stirred 1.75 h with BBr3 in CH2Cl2 to give a separable mixture of 4-[[8-fluoro-2-hydroxy-5-methoxy-4,4-dimethyl-2-(trifluoromethyl)-1,2,3,4-tetrahydronaphthalen-1-yl]amino]-2,3-dihydroisoindol-1-one and 4-[[8-fluoro-2,5-dihydroxy-4,4-dimethyl-2-(trifluoromethyl)-1,2,3,4-tetrahydronaphthalen-1-yl]amino]-2,3-dihydroisoindol-1-one.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 5 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:291437 HCAPLUS

DOCUMENT NUMBER: 143:5993

TITLE: Differential inhibition of inducible T cell cytokine secretion by potent iron chelators

AUTHOR(S): Leung, Stewart; Holbrook, April; King, Beverly; Lu, Hong-Tao; Evans, Vincent; Miyamoto, Neil; Mallari, Cornell; Harvey, Susan; Davey, Dave; Ho, Elena; Li, Wei-Wei; Parkinson, John; Horuk, Richard; **Jaroch,**

Stefan; Berger, Markus; Skuballa, Werner; West, Christopher; Pulk, Rebecca; Phillips, Gary; Bryant, Judi; Subramanyam, Babu; Schaefer, Caralee; Salamon, Hugh; Lyons, Eric; Schilling, Daniela; Seidel, Henrik; Kraetzschmar, Joern; Snider, Michael; Perez, Daniel
CORPORATE SOURCE: Berlex Biosciences, Richmond, CA, USA
SOURCE: Journal of Biomolecular Screening (2005), 10(2), 157-167
CODEN: JBISF3; ISSN: 1087-0571
PUBLISHER: Sage Publications
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Effector functions and proliferation of T helper (Th) cells are influenced by cytokines in the environment. Th1 cells respond to a synergistic effect of interleukin-12 (IL-12) and interleukin-18 (IL-18) to secrete interferon-gamma (IFN-γ). In contrast, Th2 cells respond to interleukin-4 (IL-4) to secrete IL-4, interleukin-13 (IL-13), interleukin-5 (IL-5), and interleukin-10 (IL-10). The authors were interested in identifying nonpeptide inhibitors of the Th1 response selective for the IL-12/IL-18-mediated secretion of IFN-γ while leaving the IL-4-mediated Th2 cytokine secretion relatively intact. The authors established a screening protocol using human peripheral blood mononuclear cells (PBMCs) and identified the hydrazino anthranilate compound 1 as a potent inhibitor of IL-12/IL-18-mediated IFN-γ secretion from CD3+ cells with an IC50 around 200 nM. The inhibitor was specific because it had virtually no effect on IL-4-mediated IL-13 release from the same population of cells. Further work established that compound 1 was a potent intracellular iron chelator that inhibited both IL-12/IL-18- and IL-4-mediated T cell proliferation. Iron chelation affects multiple cellular pathways in T cells. Thus, the IL-12/IL-18-mediated proliferation and IFN-γ secretion are very sensitive to intracellular iron concentration However, the IL-4-mediated IL-13 secretion does not correlate with proliferation and is partially resistant to potent iron chelation.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 6 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:29314 HCAPLUS
DOCUMENT NUMBER: 142:134197
TITLE: Preparation of heterocyclic 2-trifluoromethylpentan-2-ols and related compounds as anti-inflammatory agents
INVENTOR(S): Berger, Markus; Baeurle, Stefan; Rehwinkel, Hartmut; Schmees, Norbert; Schaecke, Heike; Lehmann, Manfred; Krolikiewicz, Konrad; Schottelius, Arndt J. B.; Nguyen, Duy; Mengel, Anne; **Jaroch, Stefan**
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 118 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

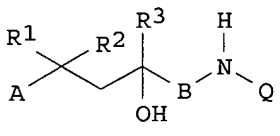
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005003098	A1	20050113	WO 2004-EP6765	20040622
WO 2005003098	B1	20050303		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,

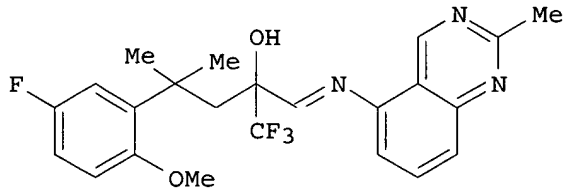
CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO,
NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ,
TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG

DE 10330358	A1	20050203	DE 2003-10330358	20030701
DE 10346939	A1	20050519	DE 2003-10346939	20031006
US 2005090559	A1	20050428	US 2004-882103	20040701
PRIORITY APPLN. INFO.:			DE 2003-10330358	A 20030701
			DE 2003-10346939	A 20031006
			US 2003-483907P	P 20030702
			US 2003-510085P	P 20031010

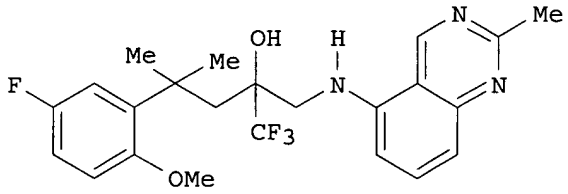
GI



I



II



III

AB Title compds. I [A = aryl, benzyl, phenylethyl, etc.; R1, R2 = H, Me, Et, etc.; R3 = (un)substituted alkoxy, alkyl, alkenyl, etc.; B = Me, Et, (un)substituted methylene, etc.; Q = (un)substituted quinazoline, quinoxaline, indazole, etc.] and their pharmaceutically acceptable salts were prepared For example, palladium-mediated hydrogenation of imine II, e.g., prepared from 4-(5-fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentanal and 5-amino-2-methylquinazoline, afforded trifluoromethylpentanol III. In a glucocorticoid receptor binding assay, compound III exhibited an IC50 value of 1.8 nM. Compds. I are claimed to be useful as antiinflammatory agents.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 7 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:658067 HCAPLUS
TITLE: Selective Glucocorticoid Receptor Agonists (SEGRAs)
AUTHOR(S): Rehwinkel, Hartmut; Schaecke, Heike; Asadullah, Khusru; Baeurle, Stefan; Berger, Markus; Hennekes, Hartwig; **Jaroch, Stefan**; Krolikiewicz, Konrad; Lehmann, Manfred; Mengel, Anne; Nguyen, Duy;

Reichel, Andreas; Rotgeri, Andrea; Schmees, Norbert; Schottelius, Arndt; Skuballa, Werner; Strehlke, Peter
CORPORATE SOURCE: Corporate Research, Schering AG, Berlin, Germany
SOURCE: Abstracts of Papers, 228th ACS National Meeting, Philadelphia, PA, United States, August 22-26, 2004 (2004), MEDI-203. American Chemical Society: Washington, D. C.
CODEN: 69FTZ8
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English

AB Glucocorticoids (GC) represent the most effective therapy for acute and chronic inflammatory disorders including allergic diseases. Their outstanding therapeutic effects, however, are often accompanied by severe and sometimes irreversible side effects, such as diabetes mellitus. Thus, there is a real need for "better" GCs, i.e. GCs with a reduced side effect profile which retain the anti-inflammatory and immunosuppressive properties of classical GCs. GCs modulate gene expression by either transactivation or transrepression mechanisms. The anti-inflammatory effects are mainly mediated via transrepression while many side effects are dependent on GC-mediated transactivation. Therefore, our aim was to identify glucocorticoid receptor (GR) ligands which preferentially induce transrepression with little transactivation. Here we show representatives of a novel class of non-steroidal compds., selective glucocorticoid receptor agonists (SEGRAs), with a significant dissociation of transactivation from transrepression activity in vitro and in vivo. The selective GR-agonists represent promising new drug candidates with an improved efficacy/tolerability profile.

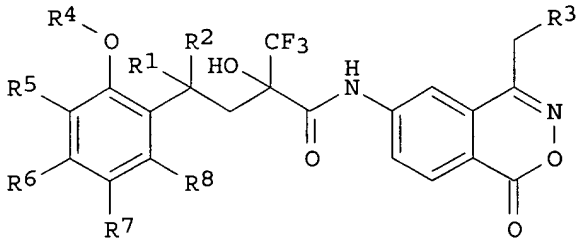
L82 ANSWER 8 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:549470 HCAPLUS
DOCUMENT NUMBER: 141:106480
TITLE: Preparation of benzoxazine derivatives as nonsteroidal inflammation inhibitors
INVENTOR(S): Schmees, Norbert; Lehmann, Manfred; Rehwinkel, Hartmut; Strehlke, Peter; **Jaroch, Stefan**; Schaecke, Heike; Schottelius, Arndt J. G.
PATENT ASSIGNEE(S): Schering AG, Germany
SOURCE: Ger. Offen., 29 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10261874	A1	20040708	DE 2002-10261874	20021220
WO 2004058733	A1	20040715	WO 2003-EP14081	20031211
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004209875	A1	20041021	US 2003-739407	20031219
PRIORITY APPLN. INFO.:			DE 2002-10261874 A	20021220

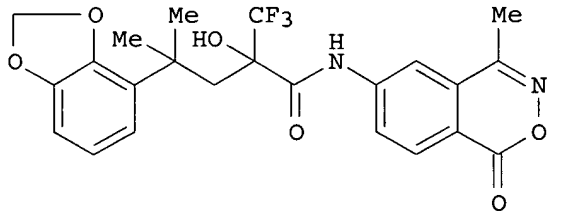
US 2003-438518P P 20030108

OTHER SOURCE(S): MARPAT 141:106480

GI



I



II

AB Title compds. I [R1-2 = alkyl, etc.; R3-4 = H, alkyl; R5-8 = H, halo, etc.] are prepared For instance, 1-(benzo[1,3]dioxol-4-yl)-1-methylethanol (preparation given) is reacted with 2-(trimethylsilyloxy)acrylic acid Et ester (CH2Cl2, SnCl4, -70°) to give 4-(benzo[1,3]dioxol-4-yl)-4-methyl-2-oxopentanoic acid Et ester. This is saponified and coupled to 6-amino-4-methyl-2,3-benzoxazin-1-one (DMA, SOCl2) to give the corresponding amide. Trifluoromethyltrimethylsilane is reacted with this intermediate and the resulting compound is desilylated to give II. II has IC50 = 1.5 nM for the glucocorticoid receptor. I are useful for the treatment and prophylaxis of illnesses, which accompany allergic and/or proliferative processes.

L82 ANSWER 9 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:51813 HCAPLUS

DOCUMENT NUMBER: 140:296856

TITLE: Fluorinated dihydroquinolines as potent n-NOS inhibitors

AUTHOR(S): **Jaroch, Stefan**; Rehwinkel, Hartmut; Holscher, Peter; Sulzle, Detlev; Burton, Gerardine; Hillmann, Margrit; McDonald, Fiona M.; Miklautz, Heribert

CORPORATE SOURCE: Corporate Research, Medicinal Chemistry, Research Center Europe, Schering AG, Berlin, D-13342, Germany

SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(3), 743-746
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 140:296856
AB Fluorinated dihydroquinolines showed reduced basicity of the amidine function. Their syntheses and potencies as neuronal nitric oxide synthase (n-NOS) inhibitors are reported.
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 10 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:39244 HCAPLUS
DOCUMENT NUMBER: 140:246499
TITLE: Dissociation of transactivation from transrepression by a selective glucocorticoid receptor agonist leads to separation of therapeutic effects from side effects
AUTHOR(S): Schaecke, Heike; Schottelius, Arndt; Doecke, Wolf-Dietrich; Strehlke, Peter; **Jaroch, Stefan**; Schmees, Norbert; Rehwinkel, Hartmut; Hennekes, Hartwig; Asadullah, Khusru
CORPORATE SOURCE: Corporate Research Business Area Dermatology, Schering AG, Berlin, Berlin, D-13342, Germany
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2004), 101(1), 227-232
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Glucocorticoids (GCs) are the most commonly used antiinflammatory and immunosuppressive drugs. Their outstanding therapeutic effects, however, are often accompanied by severe and sometimes irreversible side effects. For this reason, one goal of research in the GC field is the development of new drugs, which show a reduced side-effect profile while maintaining the antiinflammatory and immunosuppressive properties of classical GCs. GCs affect gene expression by both transactivation and transrepression mechanisms. The antiinflammatory effects are mediated to a major extent via transrepression, while many side effects are due to transactivation. Our aim has been to identify ligands of the GC receptor (GR), which preferentially induce transrepression with little or no transactivating activity. Here we describe a nonsteroidal selective GR-agonist, ZK216348, which shows a significant dissociation between transrepression and transactivation both in vitro and in vivo. In a murine model of skin inflammation, ZK216348 showed antiinflammatory activity comparable to prednisolone for both systemic and topical application. A markedly superior side-effect profile was found with regard to increases in blood glucose, spleen involution, and, to a lesser extent, skin atrophy; however, adrenocorticotropic hormone suppression was similar for both compds. Based on these findings, ZK216348 should have a lower risk, e.g., for induction of diabetes mellitus. The selective GR agonists therefore represent a promising previously undescribed class of drug candidates with an improved therapeutic index compared to classical GCs. Moreover, they are useful tool compds. for further investigating the mechanisms of GR-mediated effects.

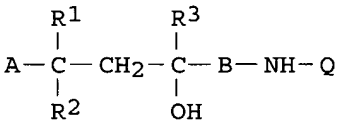
L82 ANSWER 11 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:796666 HCAPLUS
DOCUMENT NUMBER: 139:307692
TITLE: Preparation of quinoline and related compounds for use as anti-inflammatory agents
INVENTOR(S): **Jaroch, Stefan**; Lehmann, Manfred; Schmees, Norbert; Berger, Markus; Rehwinkel, Hartmut; Krolikiewicz, Konrad; Skuballa, Werner; Schaecke, Heike; Schottelius, Arndt

PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 122 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

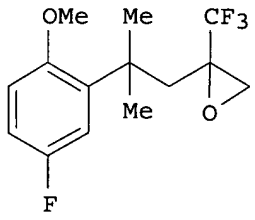
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003082827	A1	20031009	WO 2003-EP3298	20030329
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10215316	C1	20031218	DE 2002-10215316	20020402
CA 2481012	AA	20031009	CA 2003-2481012	20030329
EP 1492771	A1	20050105	EP 2003-745195	20030329
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003008967	A	20050215	BR 2003-8967	20030329
US 2004116694	A1	20040617	US 2003-405033	20030402
US 6897224	B2	20050524		
US 2005165050	A1	20050728	US 2005-59682	20050217

PRIORITY APPLN. INFO.:	DE 2002-10215316	A	20020402
	US 2002-369583P	P	20020404
	WO 2003-EP3298	W	20030329
	US 2003-405033	A3	20030402

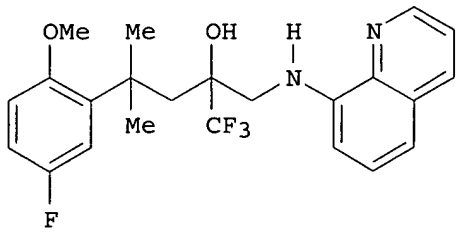
OTHER SOURCE(S): MARPAT 139:307692
GI



I



II



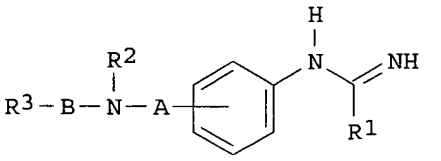
III

AB Title comounds I [A = (un)substituted aryl, benzyl, phenylethyl, etc.; R1, R2 = H, Me, Et, etc.; R3 = alkyl, fluoroalkyl; B = Me or Et substituted methylene, carbonyl; Q = (un)substituted quinoline or isoquinoline] and their pharmaceutically acceptable salts were prepared For example, condensation of 8-quinolinamine and epoxide II afforded quinoline III. Compds. I are noted useful as anti-inflammatory agents (no data provided).
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

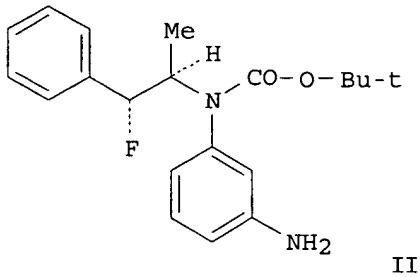
L82 ANSWER 12 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:487133 HCAPLUS
DOCUMENT NUMBER: 139:52873
TITLE: Preparation of N-phenyl-2-thiophenecarboximidamides as nitric oxide synthase inhibitors
INVENTOR(S): Rehwinkel, Hartmut; Hoelscher, Peter; **Jaroch, Stefan**; Suelzle, Detlev; Hillmann, Margrit; Burton, Gerardine Anne; McDonald, Fiona MacDougall
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: Ger. Offen., 8 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10162114	A1	20030626	DE 2001-10162114	20011212
WO 2003053914	A1	20030703	WO 2002-EP14010	20021210
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1453794	A1	20040908	EP 2002-792956	20021210
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005513124	T2	20050512	JP 2003-554631	20021210
US 2005119481	A1	20050602	US 2003-498237	20021210
PRIORITY APPLN. INFO.:			DE 2001-10162114 A	20011212
			WO 2002-EP14010 W	20021210

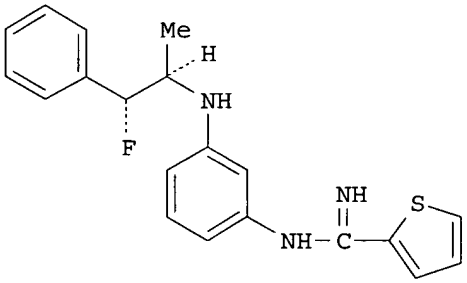
OTHER SOURCE(S): MARPAT 139:52873
GI



I



II



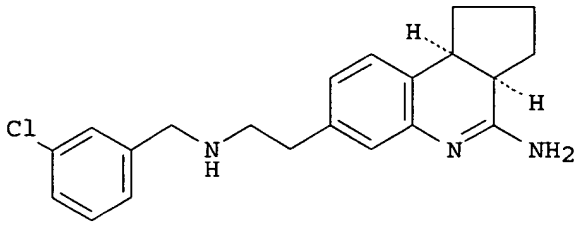
III

AB Title compds. I [R1 = (un)substituted Ph, 5-6 membered heteroaryl containing 1-3 O, S or N, atoms; R2 = H, alkyl, COO-alkyl, etc.; R3 = H, halo, (un)substituted Ph, etc.; A = CH2, CH2CH2, CH(CH3); B = halo substituted alkylene] and their pharmaceutically acceptable salts were prepared For example, coupling of aniline II, e.g., prepared from (+)-norephedrine in 6-steps, and 2-thiophenecarboximidothioic acid Me ester, followed by BOC deprotection afforded phenylthiophenecarboximidamide III dihydrochloride. Compds. I are claimed useful for the treatment of illness caused by nitric oxide synthase (no data provided).

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 13 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:405932 HCAPLUS
DOCUMENT NUMBER: 139:245882
TITLE: Dihydroquinolines with amine-containing side chains as potent n-NOS inhibitors
AUTHOR(S): **Jaroch, Stefan**; Holscher, Peter; Rehwinkel, Hartmut; Sulzle, Detlev; Burton, Gerardine; Hillmann, Margrit; McDonald, Fiona M.
CORPORATE SOURCE: Research Center Europe, Department of Medicinal Chemistry, Corporate Research, Schering AG, Berlin, D-13342, Germany
SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(12), 1981-1984
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:245882
GI



I

AB Dihydroquinolines, e.g. I. 2HCl, with aminoalkyl side chains have been synthesized and have been shown to be potent n-NOS inhibitors. A marked selectivity vs. e-NOS of up to approx. 300-fold was observed, whereas i-NOS was moderately inhibited.
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

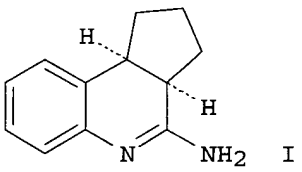
L82 ANSWER 14 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:329861 HCAPLUS
DOCUMENT NUMBER: 138:353488
TITLE: Organic chemistry 2002
AUTHOR(S): Ernst, Alexander; Wortmann, Lars; Bohlmann, Rolf; Wenz, Marion; **Jaroch, Stefan**
CORPORATE SOURCE: Switz.
SOURCE: Nachrichten aus der Chemie (2003), 51(3), 286-315
CODEN: NACHFB; ISSN: 1439-9598
PUBLISHER: Gesellschaft Deutscher Chemiker
DOCUMENT TYPE: Journal; General Review
LANGUAGE: German
AB A review on selected research works in the field of the organic chemical in 2002. Following highlights from the actual works were selected: organic solids and materials, solid-phase synthesis, peptides and peptidomimetics, pyrrole dye stuffs, photochem., radical chemical, mass spectrometry, metal organic synthesis methods, metal-free synthesis methods, natural product synthesis, biosynthesis, enzyme in the organic chemical, enzyme mechanisms/enzyme models/new proteins and their functions, artificial enzymes, supramol. chemical, pharmaceuticals, bulk products/fine chems./commodities, oncol., endocrinol., neurol.
REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 15 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:789845 HCAPLUS
DOCUMENT NUMBER: 138:348168
TITLE: SEGRAs: a novel class of anti-inflammatory compounds
AUTHOR(S): Schaecke, H.; Hennekes, H.; Schottelius, A.; **Jaroch, S.**; Lehmann, M.; Schmees, N.; Rehwinkel, H.; Asadullah, K.
CORPORATE SOURCE: Research Business Area Dermatology, Schering AG, Berlin, 13342, Germany
SOURCE: Ernst Schering Research Foundation Workshop (2002), 40(Recent Advances in Glucocorticoid Receptor Action), 357-371
CODEN: ESRWEL; ISSN: 0947-6075
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Based on the new insight into the mol. mechanisms of

glucocorticoid (GC)-mediated action, the authors and others hypothesized that activation of the glucocorticoid receptor (GR) with compds. inducing a predominant induction of transrepression over transactivation should lead to the majority of the antiinflammatory effects of GCs with less side effects. Such selective GR agonists (SEGRAs) represent a novel class of antiinflammatory compds. with a favorable effect/ side-effect profile. The authors demonstrated first as a precondition that transrepression alone is sufficient to mediate the antiinflammatory action. Second, compds. with a dissociated profile in vitro were identified, and third, their superiority was demonstrated in vivo.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 16 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:641078 HCAPLUS
DOCUMENT NUMBER: 138:153426
TITLE: Dihydroquinolines as Novel n-NOS Inhibitors
AUTHOR(S): **Jaroch, Stefan**; Holscher, Peter; Rehwinkel, Hartmut; Sulzle, Detlev; Burton, Gerardine; Hillmann, Margrit; McDonald, Fiona M.
CORPORATE SOURCE: Department of Medicinal Chemistry, Corporate Research, Berlin, D-13342, Germany
SOURCE: Bioorganic & Medicinal Chemistry Letters (2002), 12(18), 2561-2564
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Dihydroquinoline derivs., e.g. I, were synthesized by two routes and have been shown to be potent nitric oxide synthase (n-NOS) inhibitors. Selectivity vs. e-NOS was increased to approx. 100-fold through appropriate substitution at the benzene ring.

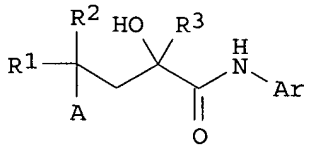
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 17 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:107324 HCAPLUS
DOCUMENT NUMBER: 136:151175
TITLE: Preparation of amido-benzoxazinone/phthalides as non-steroidal inflammation inhibitors
INVENTOR(S): **Jaroch, Stefan**; Lehmann, Manfred; Schmees, Norbert; Buchmann, Bernd; Rehwinkel, Hartmut; Droescher, Peter; Skuballa, Werner; Krolikiewicz, Konrad; Hennekes, Hartwig; Schaecke, Heike; Schottelius, Arndt
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 114 pp.
CODEN: PIXXD2

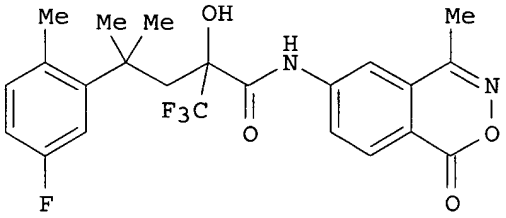
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002010143	A1	20020207	WO 2001-EP8501		20010723
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
DE 10038639	A1	20020221	DE 2000-10038639		20000728
CA 2417444	AA	20020207	CA 2001-2417444		20010723
EP 1309571	A1	20030514	EP 2001-960536		20010723
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
BR 2001012786	A	20030701	BR 2001-12786		20010723
JP 2004505068	T2	20040219	JP 2002-515874		20010723
EE 200300043	A	20041015	EE 2003-43		20010723
US 2002077356	A1	20020620	US 2001-916195		20010727
US 6777409	B2	20040817			
BG 107488	A	20030731	BG 2003-107488		20030122
NO 2003000406	A	20030327	NO 2003-406		20030127
ZA 2003001639	A	20040622	ZA 2003-1639		20030227
US 2004254249	A1	20041216	US 2004-874485		20040624
US 2005143415	A1	20050630	US 2004-957742		20041005
PRIORITY APPLN. INFO.:			DE 2000-10038639	A	20000728
			WO 2001-EP8501	W	20010723
			US 2001-916195	A1	20010727
			DE 2003-10346940	A	20031006
			US 2003-510091P	P	20031010

OTHER SOURCE(S): MARPAT 136:151175
GI



I



II

AB Title compds. I [R1-2 = H or together with the carbon to which they are attached form a 3-7 membered ring; R3 = alkyl; A = (un)substituted phenyl; Ar = (un)substituted phthalide/benzoxazinone] were prepared For example, II was prepared from 2-(5-fluoro-2-methylphenyl)-2-Me propionitrile (preparation given) in 3 steps and the enantiomers resolved by chiral chromatog. Selected examples of the invention had IC50 = 4 x 10-8 to < 3 x 10-10 M for the glucocorticoid receptor (GC) and were effective inhibiting secretion of IL-8. I are non-steroidal inflammation inhibitors and are also useful in treating dermatol., kidney, liver and gastrointestinal disorders.

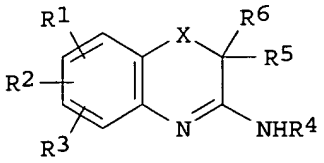
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 18 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:798206 HCAPLUS
DOCUMENT NUMBER: 135:331432
TITLE: Preparation of aminobenzoxazines and aminobenzothiazines as nitric oxide synthase inhibitors and antioxidants.
INVENTOR(S): Hoelscher, Peter; Jautelat, Rolf; Rehwinkel, Hartmut; **Jaroch, Stefan**; Suelzle, Detlev; Hillmann, Margrit; Burton, Gerardine Anne; McDonald, Fiona McDougall
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

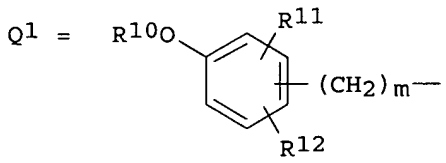
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001081324	A1	20011101	WO 2001-EP4282	20010412

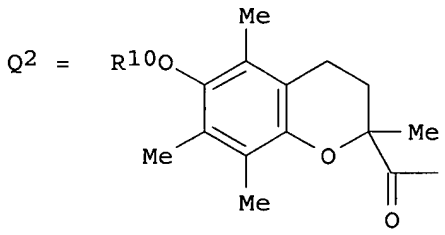
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD,

SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU,
ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: DE 2000-10021244 A 20000425
OTHER SOURCE(S): MARPAT 135:331432
GI



I





AB Title compds. [I; X = O, S; R1 = (CHR9)nNR7ANR8B, (CHR9)nNR8B, (CHR9)nB; R2 = H; R1R2 = atoms to form a 5-8 membered mono- or bicyclic (unsatd.) ring in which 1 or 2 CH2 groups can be replaced by O or CO, and which is substituted by (CHR9)rNR7ANR8B, (CHR9)nB, or (CHR9)rNR8B; R3 = H, amino; R4 = H, acyl; R5, R6 = H, (substituted) cycloalkyl, Ph, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl; R7, R8 = H, alkyl, phenylalkyl, alkoxycarbonyl, alkylcarbonyl; A = alkylene, (CH2)pQ(CH2)q; Q = cycloalkyl, indanyl, heterocycloalkyl, aryl, heteroaryl; m, n, p, q, r = 0-6; B = Q1, Q2; R9, R10 = H, alkyl; R11, R12 = H, OH, alkyl, alkoxy], were prepared as nitric oxide synthase inhibitors and antioxidants (no data). Thus, 6-[N-(4-hydroxy-3,5-di-tert-butylbenzyl)-(tert-butoxycarbonyl)aminomethyl]-2-methyl-2H-1,4-benzoxazin-3(4H)-thione (preparation given) was stirred 1 day with NH3 in MeOH to give 6-[N-(4-hydroxy-3,5-di-tert-butylbenzyl)-(tert-butoxycarbonyl)aminomethyl]-3-amino-2-methyl-2H-1,4-benzoxazine.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 19 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:798205 HCAPLUS
DOCUMENT NUMBER: 135:344492
TITLE: Preparation of benzoxazine-3-amines as neuronal nitric oxide synthase inhibitors
INVENTOR(S): Rehwinkel, Hartmut; Hoelscher, Peter; **Jaroch, Stefan**; Suelzle, Detlev; Hillmann, Margrit; Burton, Gerardine Anne; McDonald, Fiona McDougall
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001081323	A1	20011101	WO 2001-EP4281	20010412
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 10020667	A1	20011122	DE 2000-10020667	20000419
EP 1282610	A1	20030212	EP 2001-929561	20010412
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003531198	T2	20031021	JP 2001-578416	20010412
NO 2002005031	A	20021219	NO 2002-5031	20021018
US 2004006075	A1	20040108	US 2003-258016	20030723
US 6914059	B2	20050705		
PRIORITY APPLN. INFO.:			DE 2000-10020667 A	20000419
			WO 2001-EP4281 W	20010412

OTHER SOURCE(S): MARPAT 135:344492

AB R1ZNHR4 [R1 = (CHR9)nNR7Z1NHR or (CHR9)nNRR7; R = NHR7- or aryl-substituted haloalkyl; R4 = H or acyl; R7 = H, (phenyl)alkyl, alkanoyl, alkoxycarbonyl; R9 = H or alkyl; Z = (un)substituted 2H-1,4-benzoxazine- or -thiazine-m,3-diyl; Z1 = alk(en)ylene; m = 5-8; n = 0-6] were prepared as neuronal nitric oxide synthase inhibitors (no data). Thus, (R)-6-aminomethyl-2-methyl-3-oxo-2H-1,4-benzoxazine was condensed with CF3CF2CHO and the product converted in 3 steps to (R)-3-amino-2-methyl-6-[(pentafluoropropylamino)methyl]-2H-1,4-benzoxazine.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 20 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:488533 HCAPLUS

DOCUMENT NUMBER: 135:92780

TITLE: Synthesis of steroidal derivatives as lipoprotein biosynthesis inhibitors

INVENTOR(S): Brumby, Thomas; Halfbrodt, Wolfgang; **Jaroch, Stefan**; Mueller, Hans-joachim; Schoellkopf, Klaus; Heck, Reinhard

PATENT ASSIGNEE(S): Schering A.-G., Germany

SOURCE: Ger. Offen., 76 pp.
CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19963266	A1	20010705	DE 1999-19963266	19991216
PRIORITY APPLN. INFO.:			DE 1999-19963266	19991216

OTHER SOURCE(S): MARPAT 135:92780

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Steroidal derivs., such as I [R1 = H, CH2S-alkyl, CH2NHCOPh, α-CH2NHCO2CH2Ph; R1R2 = CH(OH); R1R3 = (un)substituted oxazinone ring, pyrazole ring; R2 = H; R2R4 = bond; R3 = H, OH, OCONH2, NH2, NH-alkyl, N(alkyl)2; R3R4 = O; R4 = H, CO2H, CONH2, CF3, etc.; R5 = H, OH; R5R6 = O, CH(OH), 4-carbon ring; oxygen containing C3-6-ring; R5R7 = double bond; R6 = H, hydroxy substituted C2-8-alkenyl, C1-8-alkyl-S-alkyl; R7 = H, CH2NO2; R7R8, R7R9 = double bond; R8 = H, OH, NHCO-alkyl; R9 = H, CH2S-alkyl, NHCOCMe(CH2OH)2, NHCO-(2,2,5-trimethyl-1,3-dioxolan-5-yl); R10 = H; R10R11 = O; R11 = H; R11R12 = double bond; R12 = H; R13 = H, Et; X = O, NH, N-alkyl,CH2,CH(OH),CH(CH2S-alkyl), C(OH)(CH2S-alkyl); XR3 = tetrazole], were prepared in all optically active forms, as racemates, diastereomers and diastereomeric mixts. for use as lipoprotein [Lp(a)] biosynthesis inhibitors. Thus, cholestane derivative II was prepared via a multistep synthetic sequence starting from cholest-4-en-3-one.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 21 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:152656 HCAPLUS

DOCUMENT NUMBER: 134:193440

TITLE: Preparation of benzoxazines and benzothiazines as nitric oxide synthase inhibitors.

INVENTOR(S): Hoelscher, Peter; Rehwinkel, Hartmut; **Jaroch, Stefan**; Suelzle, Detlev; Hillmann, Margrit; Burton, Gerardine Anne; McDonald, Fiona McDougall

PATENT ASSIGNEE(S): Schering AG, Germany

SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

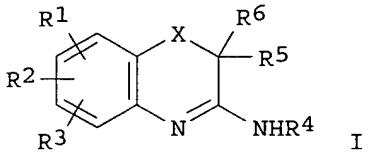
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001014347	A1	20010301	WO 2000-EP8240	20000823
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19941115	A1	20010301	DE 1999-19941115	19990825
EP 1206458	A1	20020522	EP 2000-962367	20000823
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003507460	T2	20030225	JP 2001-518435	20000823
NO 2002000883	A	20020405	NO 2002-883	20020222

PRIORITY APPLN. INFO.: DE 1999-19941115 A 19990825
WO 2000-EP8240 W 20000823

OTHER SOURCE(S): MARPAT 134:193440

GI



I

AB Title compds. [I; X = O, S, SO, SO2; R1 = (CHR9)nNR7ANR8B, (CHR9)nNR7B, etc.; R2 = H; R1R2 = atoms to form 5-8 membered mono- or bicyclic (unsatd.) (alkyl-substituted) ring substituted by R1; R3 = H, halo, NO2, cyano, CF3, OCF3, SR9, OR9, cycloalkyl, heteroaryl, COR14, (substituted) aryl, alkyl, alkenyl, alkynyl; R4 = H, acyl; R5, R6 = H, (substituted) cycloalkyl, Ph, alkyl, alkenyl, alkynyl; R7 = H, alkyl, phenylalkyl, alkoxycarbonyl, alkylcarbonyl; R8 = H; A = alkylene, alkenylene; B = C:R(CH2)pU, C:RNR15, SOR12, aryloxycarbonyl, benzyloxycarbonyl; R8B = 5-7 membered (substituted) heterocyclyl; R = O, S; n, p = 0-6; R9 = H, alkyl; R14 = H, OH, alkoxy, Ph, (substituted) alkyl, alkenyl; R15 = H, alkyl, (substituted) Ph, PhCH2], were prepared as NOS inhibitors (no data). Thus, 6-[[N-(4-chlorobenzyl)pentanethiocarboxamid-6-yl]-(tert.-butyloxycarbonyl)aminomethyl]-3-amino-2-methyl-2H-1,4-benzoxazine.

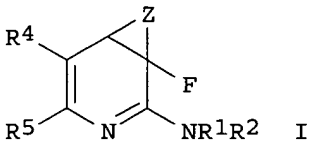
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 22 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:351501 HCAPLUS
DOCUMENT NUMBER: 132:347501
TITLE: Preparation of 3a-fluorocyclopenta[c]quinolin-4-amines and analogs as NOS inhibitors
INVENTOR(S): **Jaroch, Stefan**; Rehwinkel, Hartmut; Holscher, Peter; Sulzle, Detlev; Hillmann, Margrit; Burton, Gerardine Anne; McDonald, Fiona MacDougall
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000029381	A1	20000525	WO 1999-EP8519	19991110
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2350443	AA	20000525	CA 1999-2350443	19991110
EP 1129077	A1	20010905	EP 1999-963289	19991110
EP 1129077	B1	20050420		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9915333	A	20011009	BR 1999-15333	19991110

AU 764074	B2	20030807	AU 2000-19656		19991110
NZ 510875	A	20031031	NZ 1999-510875		19991110
AT 293605	E	20050515	AT 1999-963289		19991110
US 6579883	B1	20030617	US 2001-831514		20010510
NO 2001002328	A	20010511	NO 2001-2328		20010511
PRIORITY APPLN. INFO.:			DE 1998-19854042	A	19981113
			WO 1999-EP8519	W	19991110

OTHER SOURCE(S): MARPAT 132:347501
GI



I

AB Title compds. [I; R1,R2 = H, alkyl, alkoxy(carbonyl), acyl, etc.; R4R5 = (un)substituted CH:CHCH:CH; Z = (un)substituted (heteroatom-interrupted) alkylene] were prepared as NOS inhibitors (no data). Thus, 2,3,3a,8a-tetrahydro-1H-cyclopent[a]inden-8-one was oximated and the product subjected to Beckmann rearrangement to give, in 5 addnl. steps, I [R1 = R2 = H, R4R5 = CH:CHCH:CH, Z = (CH2)3].
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 23 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:350013 HCAPLUS
DOCUMENT NUMBER: 133:150372
TITLE: Synthesis and biological activity of leukotriene derivatives
AUTHOR(S): **Jaroch, Stefan**; Buchmann, Bernd; Skuballa, Werner
CORPORATE SOURCE: Institute of Medicinal Chemistry, Preclinical Drug Research, Schering AG, Berlin, D-13342, Germany
SOURCE: Bioorganic Chemistry (1999), 38-42. Editor(s): Diederichsen, Ulf. Wiley-VCH Verlag GmbH: Weinheim, Germany.
CODEN: 68ZQAX
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review with 11 refs. on LTB4 derivs. as leukotriene receptor antagonists.
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 24 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:291044 HCAPLUS
DOCUMENT NUMBER: 132:308345
TITLE: Preparation of thienooxazineamines and analogs as nitric oxide synthase inhibitors
INVENTOR(S): Rehwinkel, Hartmut; Holscher, Peter; **Jaroch, Stefan**; Sulzle, Detlev; Hillmann, Margrit; Burton, Gerardine Anne; Mcdonald, Fiona Macdougall
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

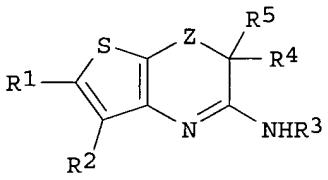
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000024746	A1	20000504	WO 1999-EP8005	19991022

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: DE 1998-19850434 A 19981027
OTHER SOURCE(S): MARPAT 132:308345
GI



I

AB Title compds. [I; R1,R2 = H, halo, cyano, acyl(amino), etc.; R1R2 = atoms to complete a ring; R3 = H or acyl; R4,R5 = H, (halo)alkyl, aryl] were prepared as nitric oxide synthase inhibitors (no data). Thus, 2-chloro-3-nitrothiophene was etherified by MeCH(OH)CO2Et and the product reductively cyclized to give, in 2 addnl. steps, I (R1-R4 = H, R5 = Me).
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 25 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:210125 HCAPLUS
DOCUMENT NUMBER: 132:251082
TITLE: Preparation of aminoalkylcyclopentaquinolines and related compounds as nitric oxide synthase inhibitors.
INVENTOR(S): **Jaroch, Stefan**; Rehwinkel, Hartmut; Holscher, Peter; Sulzle, Detlev; Hillmann, Margrit; Burton, Gerardine Anne; McDonald, Fiona McDougall
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

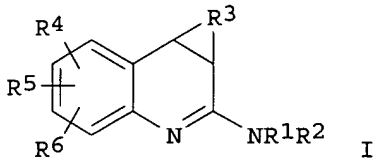
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000017167	A1	20000330	WO 1999-EP7091	19990920

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG,

MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

DE 19845830	A1	20000330	DE 1998-19845830	19980924
CA 2340990	AA	20000330	CA 1999-2340990	19990920
AU 9961955	A1	20000410	AU 1999-61955	19990920
AU 752412	B2	20020919		
EP 1115708	A1	20010718	EP 1999-948842	19990920
EP 1115708	B1	20040414		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002526478	T2	20020820	JP 2000-574077	19990920
NZ 510561	A	20031128	NZ 1999-510561	19990920
TW 565556	B	20031211	TW 1999-88116209	19990920
AT 264308	E	20040415	AT 1999-948842	19990920
PT 1115708	T	20040831	PT 1999-948842	19990920
ES 2219067	T3	20041116	ES 1999-948842	19990920
NO 2001001506	A	20010523	NO 2001-1506	20010323
US 2004127712	A1	20040701	US 2003-694845	20031029
PRIORITY APPLN. INFO.:			DE 1998-19845830 A	19980924
			WO 1999-EP7091 W	19990920
			US 2001-787848 A1	20010323

OTHER SOURCE(S): MARPAT 132:251082
GI



I

AB Title compds. [I; R1, R2 = H, alkyl, amino, cyano, acyl, OH, alkoxy, aryloxy, etc.; R3 = (unsatd.) (substituted) (heteroatom-interrupted) C1-5 alkylene; R4 = aminoalkyl; R4R5 = atoms to form a 5-6 membered ring; R5, R6 = H, halo, alkyl, CF3, OCF3, OH, alkoxy, aryloxy], were prepared for treatment of neurodegenerative disease (no data). Thus, 7-(N-tert-butoxycarbonyl-3-chlorobenzylamino)methyl-1,2,3,3a,5,9b-hexahydrocyclopenta[c]quinoline-4-thione (preparation given) was suspended in MeOH containing NH3 for 15 h to give 4-amino-7-(N-tert-butoxycarbonyl-3-chlorobenzylamino)methyl-2,3,3a,9b-tetrahydro-1H-cyclopenta[c]quinoline.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

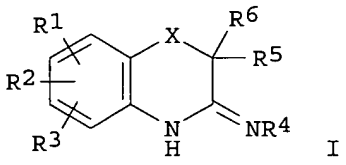
L82 ANSWER 26 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:188375 HCAPLUS
DOCUMENT NUMBER: 132:222541
TITLE: Preparation of benzoxazines and benzothiazines as nitric oxide synthase inhibitors.
INVENTOR(S): Hoelscher, Peter; Rehwinkel, Hartmut; **Jaroch, Stefan**; Suelzle, Detlev; Hillmann, Margrit; Burton, Gerardine Anne; McDougall- McDonald, Fiona

PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: Ger. Offen., 12 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19844291	A1	20000323	DE 1998-19844291	19980918
CA 2341170	AA	20000330	CA 1999-2341170	19990916
WO 2000017173	A1	20000330	WO 1999-EP7089	19990916
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9961954	A1	20000410	AU 1999-61954	19990916
AU 751381	B2	20020815		
BR 9913856	A	20010612	BR 1999-13856	19990916
EP 1114037	A1	20010711	EP 1999-948841	19990916
EP 1114037	B1	20040512		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002526481	T2	20020820	JP 2000-574083	19990916
NZ 510562	A	20030829	NZ 1999-510562	19990916
AT 266647	E	20040515	AT 1999-948841	19990916
PT 1114037	T	20040930	PT 1999-948841	19990916
ES 2221442	T3	20041216	ES 1999-948841	19990916
NO 2001001339	A	20010509	NO 2001-1339	20010316
US 6841550	B1	20050111	US 2001-787396	20010319

PRIORITY APPLN. INFO.: DE 1998-19844291 A 19980918
WO 1999-EP7089 W 19990916

OTHER SOURCE(S): MARPAT 132:222541
GI



I

AB Title compds. [I; X = O, S, SO, SO2, Se; R1 = (CHR9)nNR7ANR8B; R2 = H; R1R2 = (unsatd.) (bicyclic) 5-8 membered ring substituted with (CHR9)nNR7ANR8B and optionally substituted with alkyl; R3 = H, halo, NO2, cyano, CF3, OCF3, (substituted) aryl, heteroaryl, etc.; R4 = H, acyl; R5, R6 = H, (substituted) cycloalkyl, Ph, alkyl, alkenyl, alkynyl, etc.; R7, R8 = H, alkyl, phenylalkyl, alkoxycarbonyl, alkylcarbonyl; R9 = H, alkyl; A = alkylene, (CH2)pQ(CH2)q; B = H, (CH2)pU; n = 1-6; p, q = 0-6; Q = cycloalkyl, indanyl, heterocycloalkyl, heteroaryl, etc.; U = H, cycloalkyl, indanyl, bicycloalkyl, aryl, heteroaryl], were prepared as

nitric oxide synthase inhibitors (no data). Thus, 6-[[3-(tert-butoxycarbonyl)aminomethyl]benzyl-(tert-butoxycarbonyl)aminomethyl]-2-methyl-1,4-benzoxazin-3-thione (preparation given) was stirred with NH3 in MeOH to give 75% 6-[[3-(tert-butoxycarbonyl)aminomethyl]benzyl-(tert-butoxycarbonyl)aminomethyl]-3-amino-2-methyl-1,4-benzoxazine.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

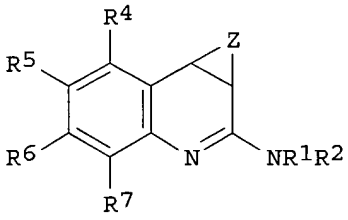
L82 ANSWER 27 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:750955 HCAPLUS
DOCUMENT NUMBER: 132:194536
TITLE: Studies towards a total synthesis of sarains A-C. Stereospecific condensation of α,β-unsaturated esters with the phenyl oxazoline derivative of threonine. [Erratum to document cited in CA130:311959]
AUTHOR(S): **Jaroch, Stefan**; Matsuoka, Richard T.; Overman, Larry E.
CORPORATE SOURCE: Department of Chemistry, University of California, Irvine, CA, 92697-2025, USA
SOURCE: Tetrahedron Letters (1999), 40(49), 8719
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The correct structure is given for product on page 1275.

L82 ANSWER 28 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:529135 HCAPLUS
DOCUMENT NUMBER: 131:157716
TITLE: Preparation of annelated 3,4-dihydroquinolines as nitric oxide synthase inhibitors
INVENTOR(S): **Jaroch, Stefan**; Rehwinkel, Hartmut; Holscher, Peter; Sulzle, Detlev; Hillmann, Margrit; Burton, Gerardine Anne; McDonald, Fiona Mcdougall
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9941240	A1	19990819	WO 1999-DE382	19990209
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19806348	A1	19990819	DE 1998-19806348	19980212
AU 9929211	A1	19990830	AU 1999-29211	19990209
EP 1054869	A1	20001129	EP 1999-910126	19990209
EP 1054869	B1	20040922		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

JP 2002503652	T2	20020205	JP 2000-531435		19990209
AT 277018	E	20041015	AT 1999-910126		19990209
PT 1054869	T	20050228	PT 1999-910126		19990209
ES 2229688	T3	20050416	ES 1999-910126		19990209
US 6391887	B1	20020521	US 2000-622259		20000814
PRIORITY APPLN. INFO.:			DE 1998-19806348	A	19980212
			WO 1999-DE382	W	19990209

OTHER SOURCE(S): MARPAT 131:157716
GI



I

AB Title compds. [I;R1,R2 = H, alkyl, acyl, etc.; R4-R7 = H, halo, alkyl, alkoxy, etc.; Z = (un)substituted (heteroatom-containing)(oxo)alkylene] were prepared Thus, 3-(MeO)C6H4NCO was condensed with 1-morpholinocyclopentene to give 3-(MeO)C6H4NHCOR (R = 2-oxocyclopentenyl) which was cyclized and the product converted in 3 steps to I [R1 = R2 = R4 = R4 = R7 = H, R6 = OMe, Z = (CH2)3]. Data for biol. activity of I were given.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

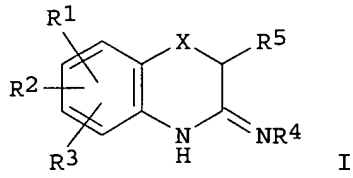
L82 ANSWER 29 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:194132 HCAPLUS
DOCUMENT NUMBER: 130:237577
TITLE: Benzoxazine and benzothiazine derivatives and their use as nitric oxide synthase inhibitors
INVENTOR(S): Holscher, Peter; Rehwinkel, Hartmut; **Jaroch, Stefan**; Suelzle, Detlev
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9912915	A1	19990318	WO 1998-DE2690	19980908
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
ZA 9808168	A	19990308	ZA 1998-8168	19980907
CA 2303440	AA	19990318	CA 1998-2303440	19980908
AU 9910220	A1	19990329	AU 1999-10220	19980908

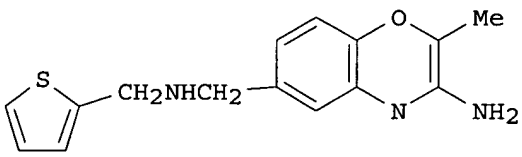
AU 741297	B2	20011129			
EP 1015437	A1	20000705	EP 1998-952562		19980908
EP 1015437	B1	20031203			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
BR 9812160	A	20000718	BR 1998-12160		19980908
TR 200000637	T2	20000721	TR 2000-200000637		19980908
JP 2001515892	T2	20010925	JP 2000-510723		19980908
TW 457236	B	20011001	TW 1998-87114926		19980908
NZ 503230	A	20020328	NZ 1998-503230		19980908
AT 255567	E	20031215	AT 1998-952562		19980908
CN 1136202	B	20040128	CN 1998-810925		19980908
PT 1015437	T	20040430	PT 1998-952562		19980908
IL 134930	A1	20040620	IL 1998-134930		19980908
ES 2212361	T3	20040716	ES 1998-952562		19980908
NO 2000001149	A	20000505	NO 2000-1149		20000307
MX 200002377	A	20001029	MX 2000-2377		20000308
US 6365736	B1	20020402	US 2000-581119		20000615
PRIORITY APPLN. INFO.:			DE 1997-19740386	A	19970908
			DE 1998-19826232	A	19980605
			WO 1998-DE2690	W	19980908

OTHER SOURCE(S): MARPAT 130:237577

GI



I



II

AB Title compds. I [X = O, SOm, Se; m = 0-2; R1 = NO2, CN, CF3, OCF3, (un)substituted SO2NH2, CONH2, NHC(:NH)R6, NHCSNH2, NHCONH2, NH2, CO2H, acyl, aryl, heteroaryl, alkyl, alkenyl, alkynyl, cycloalkyl; R2 = H; R1R2 = atoms required to complete a mono- or polycyclic ring system; R3 = H, halogen, (un)substituted SH, OH, R1; R4 = H, acyl; R5 = (un)substituted cycloalkyl, aryl, alkyl, alkenyl, alkynyl; R6 = (un)substituted alkyl, aryl, NH2, NHMe, NHCN] were prepared for use as NO synthase inhibitors (no data). Thus, 6-formyl-2-methyl-1,4-benzoxazin-3-one was reductively aminated with 2-aminomethylthiophene, N-tert.-butoxycarbonylated, treated with Lawesson's reagent, and deblocked to give the benzoxazine II.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 30 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:118553 HCAPLUS

DOCUMENT NUMBER: 130:311959

TITLE: Studies towards a total synthesis of sarains A-C.

Stereospecific condensation of α,β-unsaturated esters with the phenyl oxazoline derivative of threonine

AUTHOR(S): **Jaroch, Stefan**; Matsuoka, Richard T.; Overman, Larry E.

CORPORATE SOURCE: Department of Chemistry, University of California, Irvine, CA, 92697-2025, USA

SOURCE: Tetrahedron Letters (1999), 40(7), 1273-1276
CODEN: TELEAY; ISSN: 0040-4039

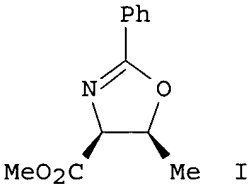
PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

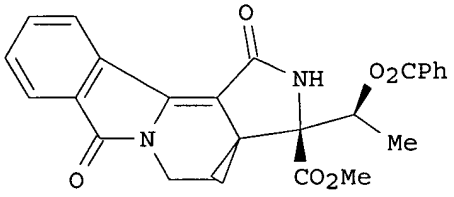
LANGUAGE: English

OTHER SOURCE(S): CASREACT 130:311959

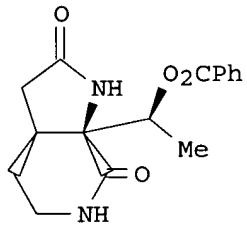
GI



I



II



III

AB Michael addition of the lithium enolate of oxazoline I to E and Z α,β-unsatd. esters proceeded with high enoate facial selectivity to yield enantiopure oxazoline derivs. of disubstituted glutamic acids. When a Z enoate was used the C4'-C3'-C7' stereotriad II and III of sarains A-C could be generated.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 31 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:789123 HCAPLUS

DOCUMENT NUMBER: 130:24908

TITLE: syntheses and activities of leukotriene B4 derivatives for use in treatment of dermatitis

INVENTOR(S): Buchmann, Bernd; Frohlich, Wolfgang; Giesen, Claudia; Hennekes, Hartwig; **Jaroch, Stefan**; Skuballa, Werner

PATENT ASSIGNEE(S): Schering A.-G., Germany

SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

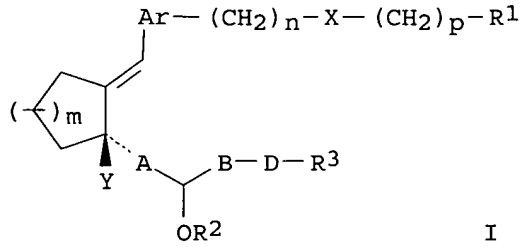
LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9852916	A1	19981126	WO 1998-EP3140	19980522
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19722845	A1	19981210	DE 1997-19722845	19970523
AU 9879162	A1	19981211	AU 1998-79162	19980522
PRIORITY APPLN. INFO.:			DE 1997-19722845 A	19970523
			WO 1998-EP3140 W	19980522

OTHER SOURCE(S): MARPAT 130:24908
GI



I

AB Syntheses of leukotriene B4 derivs. (I) [R1 = CH2OH, CH3, CF3, CO2R4, CONR5R6; R2 = H, an organic acid radical with 1-15 C atoms; R3 = H, alkyl, cycloalkyl, aryl, heteroaryl; R4 = H, alkyl, cycloalkyl, aryl, CH2-CO-aryl; A = (E,E)-CH=CH-CH=CH, (E)-CH2CH2-CH=CH-, (CH2)4; B = alkylene group, CH2cycloalkyl, cycloalkylCH2; D = bond, O, S, -C.tplbond.C-, -CH=CR7; R5,R6 = H; R7 = alkyl, Cl, Br; Ar = aromatic ring; m = 1-3, n = 0-5, p = 0-5; X = bond, O, S, -CH=CH-; Y = alkyl, cycloalkyl] as well as salts with physiol. acceptable bases and cyclodextrin clathrates are described. I can be used as dermatic agents.

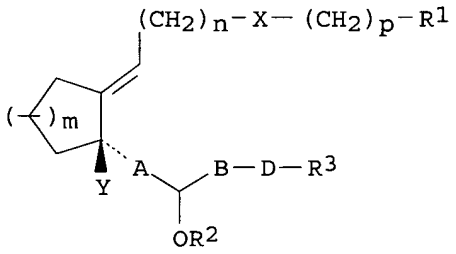
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 32 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:789122 HCAPLUS
DOCUMENT NUMBER: 130:24907
TITLE: syntheses of leukotriene B4 derivatives, in particular 7-methylcyclohexyl-LTB4 antagonists, for use in treatment of dermatitis
INVENTOR(S): Buchmann, Bernd; Frohlich, Wolfgang; Giesen, Claudia; Hennekes, Hartwig; **Jaroch, Stefan**; Skuballa, Werner
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9852914	A1	19981126	WO 1998-EP3138	19980522
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19722846	A1	19981224	DE 1997-19722846	19970523
CA 2291112	AA	19981126	CA 1998-2291112	19980522
AU 9880202	A1	19981211	AU 1998-80202	19980522
AU 735747	B2	20010712		
EP 983234	A1	20000308	EP 1998-928323	19980522
EP 983234	B1	20020703		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001525842	T2	20011211	JP 1998-549988	19980522
AT 220059	E	20020715	AT 1998-928323	19980522
NO 9905720	A	20000121	NO 1999-5720	19991122
US 6340706	B1	20020122	US 2000-424449	20000310
PRIORITY APPLN. INFO.:			DE 1997-19722846 A	19970523
			WO 1998-EP3138 W	19980522

OTHER SOURCE(S): MARPAT 130:24907
GI



I

AB Syntheses of leukotriene B4 derivs. (I) [R1 = CH2OH, CH3, CF3, CO2R4, CONR5R6; R2 = H or an organic acid radical with 1-15 C atoms; R3 = H; R4 = H, alkyl, cycloalkyl, halogen (un)substituted aryl, Ph, alkyl, alkoxy, CH2F, CH2Cl, F3C, CO2H, OH, CH2COaryl, heteroaryl; A = (E,E)-CH=CH-CH=CH, (E)-CH2CH2-CH=CH, (CH2)4; B = linear or branched-chain alkylene group, cycloalkylmethyl, methylcycloalkyl; D = direct bonding, O, S, -C.tplbond.C-, -CH=CR7, direct bonding with B; R5,R6 = H, (un)substituted OH, (un)substituted SO2; R7 = H, alkyl, Cl, Br; m = 1-3; n = 0-5; p = 0-5; X = bond, O, S; Y = alkyl, cycloalkyl] as well as salts, having physiol. compatible bases and their cyclodextrin clathrates are described. I are useful in the treatment of dermatitis.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 33 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:789121 HCAPLUS
DOCUMENT NUMBER: 130:24906
TITLE: Preparation of leukotriene B4 antagonists, in particular 3-carbatetrahydronaphthalene LTB4 antagonists
INVENTOR(S): Buchmann, Bernd; Frohlich, Wolfgang; Giesen, Claudia;

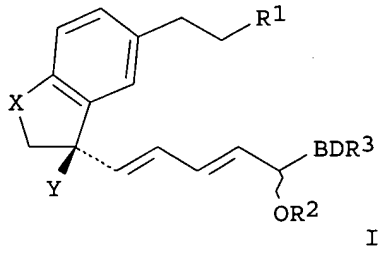
Hennekes, Hartwig; **Jaroch, Stefan**; Skuballa, Werner

PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

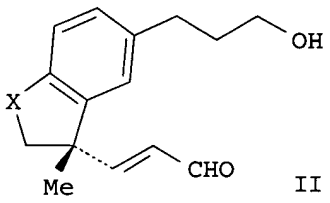
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9852912	A2	19981126	WO 1998-EP3136	19980522
WO 9852912	A3	19990225		
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19722853	A1	19981210	DE 1997-19722853	19970523
AU 9881070	A1	19981211	AU 1998-81070	19980522
PRIORITY APPLN. INFO.:			DE 1997-19722853 A	19970523
			WO 1998-EP3136 W	19980522

OTHER SOURCE(S): CASREACT 130:24906; MARPAT 130:24906

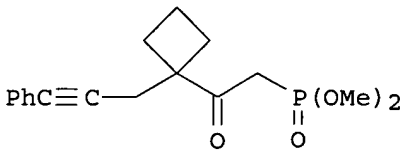
GI



I



II



III

AB The invention relates to leukotriene B4 antagonists I [R1 = CH2OH, CO2R4, CONR5R6; R2 = H, acyl; R3 = H, substituted alkyl, cycloalkyl, aryl, heteroaryl; R4 = H, alkyl, cycloalkyl, substituted aryl, heteroaryl; R5, R6 = H, (un)substituted alkyl; R5 = (un)substituted alkanoyl, SO2R8, with R6 = H; R7 = H, alkyl, Cl, Br; R8 = R3; B = (un)fluorinated alkenyl, CH2C:(CH2)n, C:(CH2)nCH2, ; D = bond, O, S, C.tplbond.C, CH:CHR7; BD = bond; X = (CH2)m; Y = (un)substituted alkyl, cycloalkyl, aryl; m = 1 - 3; n = 2 - 5], a method for their production and the pharmaceutical use thereof. Thus, (RS)-I [R1 = CH2OH, R2 = H, R3 = CH2C.tplbond.CPh, B = C(:O), D = cyclobutane-1,1-diyl, X = CH2CH2, Y = Me] was prepared via a Wittig coupling

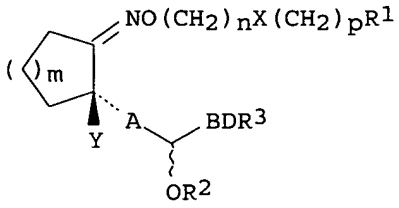
of aldehyde II (X = CH2CH2) and phosphonate III. I were tested in an LTB4 receptor competitive binding assay and for their effect on LTB4-induced chemotaxis.

L82 ANSWER 34 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:771346 HCAPLUS
DOCUMENT NUMBER: 130:24803
TITLE: Preparation of 1-alkoximino-2-alkadienynylcyclohexanes as leukotriene B4 antagonists.
INVENTOR(S): **Jaroch, Stefan**; Skuballa, Werner; Buchmann, Bernd; Froehlich, Wolfgang; Giesen, Claudia; Hennekes, Hartwig
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: Ger. Offen., 28 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

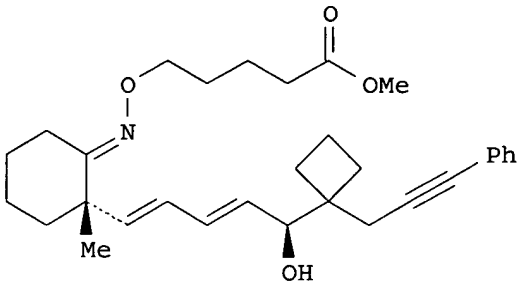
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19722848	A1	19981126	DE 1997-19722848	19970523
CA 2291123	AA	19981126	CA 1998-2291123	19980522
WO 9852915	A2	19981126	WO 1998-EP3139	19980522
WO 9852915	A3	19990225		
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9881071	A1	19981211	AU 1998-81071	19980522
AU 736132	B2	20010726		
EP 983235	A2	20000308	EP 1998-930743	19980522
EP 983235	B1	20020703		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002500646	T2	20020108	JP 1998-549989	19980522
AT 220060	E	20020715	AT 1998-930743	19980522
NO 9905721	A	20000120	NO 1999-5721	19991122
US 6160012	A	20001212	US 2000-423336	20000327

PRIORITY APPLN. INFO.: DE 1997-19722848 A 19970523
WO 1998-EP3139 W 19980522

OTHER SOURCE(S): MARPAT 130:24803
GI



I



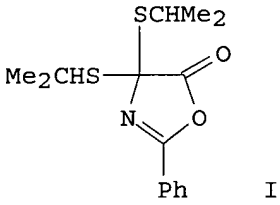
II

AB Title compds. [I; R1 = H, CF3, CH2OH, CO2R4, CONR5R6; R2 = H, organic acid residue; R3 = H, (substituted) alkyl, cycloalkyl, aryl, heteroaryl; R4 = H, alkyl, cycloalkyl, (substituted) aryl, arylcarbonylmethyl, heterocyclyl; A = trans, trans CH:CHCH:CH, CH2CH2CH:CH, tetramethylene; B = (fluoro-substituted) C1-10 alkylene, 1,1-cycloalkylmethyl; D = bond, O, S, C.tplbond.C, CH:CR7; BD = bond; R5, R6 = H, alkyl, hydroxyalkyl, etc.; R7 = H, alkyl, Cl, Br; m = 1-3; n, p = 0-5], were prepared as drugs (no data). Thus, (2S)-2-[(5S)-tert-butyldimethylsilyloxy-9-phenyl-6,6-trimethylene-1,3-nonadien-8-ynyl]-2-methylcyclohexanone was stirred with hydroxylammonium sulfate in THF/MeOH/H2O to give the oxime, which in DMF was treated with NaH and then with Me 5-bromovalerate to give the oxime ether, which was desilylated with Bu4NF in THF to give title compound (II).

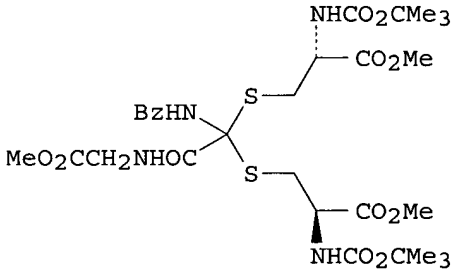
L82 ANSWER 35 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:133629 HCAPLUS
DOCUMENT NUMBER: 122:81906
TITLE: Application of α-chloroglycine residues for the modification of oligopeptides
AUTHOR(S): Steglich, Wolfgang; Jager, Martin; **Jaroch, Stefan**; Zistler, Peter
CORPORATE SOURCE: Institut fuer Organische Chemie der Universitaet, Muenchen, 80333, Germany
SOURCE: Pure and Applied Chemistry (1994), 66(10/11), 2167-70
CODEN: PACHAS; ISSN: 0033-4545
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB Review with 5 refs. New reactions of peptides incorporating electrophilic glycine equivs. are described including cycloaddns. and a novel dimerization reaction. The stereochem. of the addition of nucleophiles to this type of compds. is discussed.

L82 ANSWER 36 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:409961 HCAPLUS
DOCUMENT NUMBER: 121:9961
TITLE: Synthesis and reactions of α,α-dichloroglycyl peptides

AUTHOR(S): **Jaroch, Stefan**; Schwarz, Thomas; Steglich, Wolfgang; Zistler, Peter
CORPORATE SOURCE: Inst. Chem., Univ. Munich, Munich, D-80333, Germany
SOURCE: Angewandte Chemie (1993), 105(12), 1803-5 (See also Angew. Chem., Int. Ed. Engl., 1993, 32(12), 1771-2)
CODEN: ANCEAD; ISSN: 0044-8249
DOCUMENT TYPE: Journal
LANGUAGE: German
OTHER SOURCE(S): CASREACT 121:9961
GI



I



II

AB BzNHCCl2CO-X-OMe (X = Ala, Gly) were prepared from the oxazolidone I and H-X-OMe, followed by treatment of BzNHC(SCHMe2)2CO-X-OMe with SO2Cl2. BzNHCCl2CO-X-OMe reacted with thiols to give, e.g., the cysteine derivative II.

L82 ANSWER 37 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:218483 HCAPLUS
DOCUMENT NUMBER: 120:218483
TITLE: Generation of α-acetoxyglycine residues with peptide chains: a new strategy for the modification of oligopeptides
AUTHOR(S): Apitz, Gregor; Jaeger, Martin; **Jaroch, Stefan**; Kratzel, Martin; Schaeffeler, Lothar; Steglich, Wolfgang
CORPORATE SOURCE: Inst. Org. Chem., Univ. Muenchen, Munich, D-8000/2, Germany
SOURCE: Tetrahedron (1993), 49(36), 8223-32
CODEN: TETRAB; ISSN: 0040-4020
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 120:218483

AB Seryl and threonyl peptides are converted into α-acetoxyglycyl peptides by treatment with lead tetraacetate. Reaction of these acetoxy derivs. or the more reactive α-chloroglycyl peptides with thiols, dithiols and carbohydrates allows the attachment of such units to peptide chains. The reaction of α-chloroglycyl peptides with amino acid esters and enamines proceeds with high stereoselectivity and yields peptides with N,N-acetal and (2-oxocyclohexyl)glycine moieties, resp.

=> => d stat que l84 nos
L66 STR
L68 601 SEA FILE=REGISTRY SSS FUL L66
L69 STR
L70 12 SEA FILE=REGISTRY SUB=L68 SSS FUL L69

```
L71           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L70
L72         589 SEA FILE=REGISTRY ABB=ON  PLU=ON  L68 NOT L70
L73         102 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L72
L74          86 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L73 AND PD=<OCTOBER 24, 2003
L75          86 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L74 NOT L71
L76          20 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L75 AND PATENT/DT
L77          66 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L75 NOT L76
L79          19 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("DUNNING L"/AU OR "DUNNING L
                A"/AU OR "DUNNING L K"/AU OR "DUNNING L KAY"/AU OR "DUNNING L
                L"/AU OR "DUNNING L M"/AU OR "DUNNING LAURA"/AU)
L80          18 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L79 NOT (L71 OR L76 OR L77)
L81          38 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("JAROCH S"/AU OR "JAROCH
                STEFAN"/AU)
L82          37 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L81 NOT (L71 OR L76 OR L77 OR
                L80)
L83          32 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("KOCHANNY M"/AU OR "KOCHANNY
                MONICA"/AU OR "KOCHANNY MONICA J"/AU OR "KOCHANNY MONICA
                JEAN"/AU)
L84          31 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L83 NOT (L71 OR L76 OR L77 OR
                L80 OR L82)


=>
=>

=> d ibib abs l84 1-31

L84  ANSWER 1 OF 31  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:        2005:739895  HCAPLUS
TITLE:                   Identification of potent and selective inhibitors of
                         rhosphoinositide-dependent kinase-1 (PDK1)
AUTHOR(S):               Arnaiz, Damian O.; Feldman, Richard I.; Bryant, Judi;
                         Buckman, Brad O.; Chang, Zheng; Khim, Seock-Kyu;
                         Kosemund, Dirk; Yuan, Shendong; Adler, Marc; Alicke,
                         Bruno; Biroc, Sandra L.; Ho, Elena; Lentz, Dao;
                         Polokoff, Mark A.; Shen, Jun; Subramanyam, Babu;
                         Walters, Janette; Whitlow, Marc; Wu, James M.; Zhu,
                         Daguang; Kochanny, Monica J.; Phillips, Gary
                         B.
CORPORATE SOURCE:        Department of Chemistry, Berlex Biosciences, Richmond,
                         CA, 94804, USA
SOURCE:                  Abstracts of Papers, 230th ACS National Meeting,
                         Washington, DC, United States, Aug. 28-Sept. 1, 2005
                         (2005), MEDI-387.  American Chemical Society:
                         Washington, D. C.
                         CODEN: 69HFCL
DOCUMENT TYPE:           Conference; Meeting Abstract; (computer optical disk)
LANGUAGE:                English
AB   The PI 3-Kinase/ PDK1/Akt signaling pathway plays a key role in cancer
     cell growth, survival, and tumor angiogenesis and represents a promising
     target for anti-cancer drugs.  High-throughput screening using a PDK1
     mediated AKT2 activation assay identified several compds. with activity
     less than 500 nM.  The most potent was compound 1 (IC50 = 27 nM).  Further
     testing determined that this compound was an inhibitor of PDK1.  Although 1
was a
     potent inhibitor, it had poor selectivity against other kinases, and
     non-optimal ADME properties.  Optimization of the aniline at C-2 afforded
     BX-912 which had improved potency (IC50 = 6 nM) and selectivity against
     other kinases.  BX-912 also had good pharmacokinetic properties after iv
     dosing, but was not orally bioavailable.  Optimization of the histamine
```

sidechain at C-4 afforded BX-320. BX-320 was less potent (IC50 = 25 nM) than BX-912, but had superior selectivity and pharmacokinetic properties. BX-320 inhibited the growth of LOX melanoma tumors in the lungs of nude mice.

L84 ANSWER 2 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:418629 HCAPLUS
DOCUMENT NUMBER: 143:109159
TITLE: Novel Small Molecule Inhibitors of 3-Phosphoinositide-dependent Kinase-1
AUTHOR(S): Feldman, Richard I.; Wu, James M.; Polokoff, Mark A.; **Kochanny, Monica J.**; Dinter, Harald; Zhu, Daguang; Biroc, Sandra L.; Alicke, Bruno; Bryant, Judi; Yuan, Shendong; Buckman, Brad O.; Lentz, Dao; Ferrer, Mike; Whitlow, Marc; Adler, Marc; Finster, Silke; Chang, Zheng; Arnaiz, Damian O.
CORPORATE SOURCE: Department of Cancer Research, Berlex Biosciences, Richmond, CA, 94804, USA
SOURCE: Journal of Biological Chemistry (2005), 280(20), 19867-19874
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The phosphoinositide 3-kinase/3-phosphoinositide-dependent kinase 1 (PDK1)/Akt signaling pathway plays a key role in cancer cell growth, survival, and tumor angiogenesis and represents a promising target for anticancer drugs. Here, the authors describe three potent PDK1 inhibitors, BX-795, BX-912, and BX-320 (IC50 = 11-30 nM) and their initial biol. characterization. The inhibitors blocked PDK1/Akt signaling in tumor cells and inhibited the anchorage-dependent growth of a variety of tumor cell lines in culture or induced apoptosis. A number of cancer cell lines with elevated Akt activity were >30-fold more sensitive to growth inhibition by PDK1 inhibitors in soft agar than on tissue culture plastic, consistent with the cell survival function of the PDK1/Akt signaling pathway, which is particularly important for unattached cells. BX-320 inhibited the growth of LOX melanoma tumors in the lungs of nude mice after injection of tumor cells into the tail vein. The effect of BX-320 on cancer cell growth in vitro and in vivo indicates that PDK1 inhibitors may have clin. utility as anticancer agents.
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 3 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:371024 HCAPLUS
DOCUMENT NUMBER: 142:430132
TITLE: Preparation of indolinone derivatives and their use in treating disease-states such as cancer
INVENTOR(S): Arnaiz, Damian; Bryant, Judi; Chou, Yuo-Ling; Feldman, Richard; Hrvatin, Paul; Islam, Imadul; **Kochanny, Monica**; Lee, Wheeseong; Polokoff, Mark; Yu, Hongyi; Yuan, Shendong
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: U.S. Pat. Appl. Publ., 63 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005090541	A1	20050428	US 2004-972023	20041022
WO 2005040116	A2	20050506	WO 2004-US35262	20041022
WO 2005040116	A3	20050616		

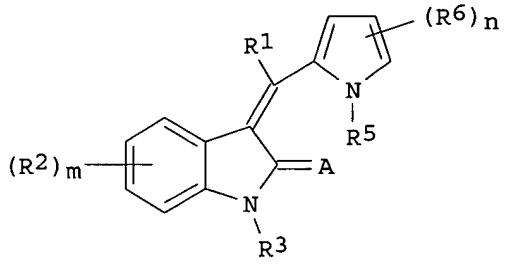
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-514081P P 20031024

OTHER SOURCE(S): MARPAT 142:430132

GI



I

AB 3-(2-Pyrrolylmethylene)indolinone derivs. (I) [R1 = H, alkyl, C(O)OR7, C(O)N(R7)2, each (un)substituted aryl, aralkyl, or heterocyclyl; R2 = alkyl, alkenyl, alkynyl, halo, haloalkyl, haloalkenyl, cyano, -R8-OR7, -R8-N(R7)2, -R8-C(O)OR7, -R8-C(O)N(R7)2, -R8-S(O)tN(R7)2, -R8-N(R7)S(O)tR7, -R8-N(R7)S(O)tN(R7)2, -R8-N(R7)S(O)tN(R7)C(O)OR7, -R8-N(R7)C(O)R7, -R8-N(R7)-R8-C(O)OR7, -R8-N(R7)C(O)N(R7)2, -R8-N(R7)C(O)-R9-N(R7)2, -R8-N(R7)-R9-C(O)N(R7)2, -R8-N(R7)C(O)-R8-N(R7)-R8-C(O)OR7, -R8-N(R7)C(O)-R8-N(R7)-R8-C(O)-R8-N(R7)2, each (un)substituted heterocyclyl or cyclic ureido group, etc.; (where t = 1 or 2) R3 is hydrogen, alkyl or aralkyl; R5 = H, alkyl, aryl, aralkyl, -C(O)R11, -S(O)2R11; R6 = alkyl, alkenyl, alkynyl, halo, haloalkyl, cyano, nitro, each (un)substituted aryl, aralkyl, or heterocyclyl, -R9-OR7, -R8-C(O)OR7, -R8-C(O)N(R7)2, -R8-C(O)R7, -R8-N(R7)2, -R8-N(R7)C(O)R7, -R8-C(O)-R9-N(R7)2, -R8-N(R7)-R8-C(O)OR7, -R8-N(R7)C(O)N(R7)2, etc.; R7 = H, haloalkyl, each (un)substituted alkyl, aryl, aralkyl, heterocyclyl, or heterocyclylalkyl; R8 = a bond or a straight or branched alkylene chain; R11 = haloalkyl, each (un)substituted alkyl, aryl, aralkyl, heterocyclyl, or heterocyclylalkyl] as a single stereoisomer, a mixture of stereoisomers, a solvate or a polymorph or pharmaceutically acceptable salts thereof are prepared These compds. are useful in treating mammal having disease-states alleviated by the inhibition of phosphoinositide-dependent kinase-1 (PDK-1) activity. Thus, a solution of 5-methoxyindolin-2-one (0.41 g) and 2-pyrrolecarboxaldehyde (0.25 g) in ethanol (5 mL) was treated with piperidine (0.05 g). The reaction mixture was then heated to 85° for

3 h, cooled to ambient temperature, and chromatographed on silica gel (12 g) using 3:1 hexane/ethyl acetate to give 5-methoxy-3-[(pyrrol-2-yl)methylene]indolin-2-one (0.48 g).

L84 ANSWER 4 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:189673 HCAPLUS
TITLE: Predicted CCR1 structure and binding modes of CCR1 antagonists
AUTHOR(S): Schlyer, Sabine K.; **Kochanny, Monica**; Phillips, Gary; Koovakkat, Sunil; Horuk, Richard; Trabanino, Rene; Floriano, Wely B.; Hall, Spencer E.; Vaidehi, N.; Goddard, William A.
CORPORATE SOURCE: Department of Medicinal Chemistry, Berlex Biosciences, Richmond, CA, 94804, USA
SOURCE: Abstracts of Papers, 229th ACS National Meeting, San Diego, CA, United States, March 13-17, 2005 (2005), COMP-319. American Chemical Society: Washington, D. C.
CODEN: 69GQMP
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB GPCRs comprise an important family of drug targets, but there is only one crystal structure available, from which homol. models can be derived. However, low sequence homol. to bovine rhodopsin, may introduce large uncertainties into structural models, and thus may adversely affect our understanding of ligand-receptor interactions. In order to address issues of species selectivity and cross reactivity, more accurate models of GPCRs are needed, which can guide us in the design of more specific and potent ligands. We present a method to model GPCRs from first principles. The transmembrane domains and their relative translation are determined only from the protein sequence, and the helix packing, i. e. the rotations of the helixes within the membrane is solely based on phys. and energetic criteria. No assumptions are made about the location and size of the ligand binding site. The binding site is determined by an automated procedure, which has the advantage of possibly identifying multiple binding sites or alternative binding sites different from the retinol binding site in rhodopsin. The structure building and docking methods have been validated using the bovine rhodopsin crystal structure and exptl. binding and mutation data for a number of other GPCRs. In this work, we present a structural model of the interaction of a non peptide antagonist of CCR1 that was constructed using the above described methods. We have validated this model using known inhouse affinity data and are currently completing virtual screening efforts. Mutation studies are also underway. These approaches are useful since the CCR1 antagonist is currently being evaluated in phase II clin. trials. The receptor model will provide us with a detailed understanding of the receptor-ligand interactions. This can be the basis for guiding future studies aimed at identifying second generation CCR1 antagonists.

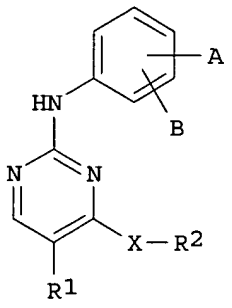
L84 ANSWER 5 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:467870 HCAPLUS
DOCUMENT NUMBER: 141:38625
TITLE: Preparation of Chk-, pdk- and akt-inhibitory pyrimidines
INVENTOR(S): Bryant, Judi; **Kochanny, Monica**; Yuan, Shendong; Khim, Seock-Kuy; Buckman, Brad; Arnaiz, Damian; Boemer, Ulf; Briem, Hans; Esperling, Peter; Huwe, Peter; Kuhnke, Joachim; Schaefer, Martina; Wortmann, Lars; Kosemund, Dirk; Eckle, Emil; Feldman, Richard; Phillips, Gary

PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 293 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004048343	A1	20040610	WO 2003-EP13443	20031128
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2502970	AA	20040610	CA 2003-2502970	20031128
US 2004186118	A1	20040923	US 2003-722591	20031128
EP 1565446	A1	20050824	EP 2003-780086	20031128
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.: EP 2002-26607 A 20021128
WO 2003-EP13443 W 20031128

OTHER SOURCE(S): MARPAT 141:38625
GI



I

AB The title compds. [I; A, B = CN, halo, H, OH, etc.; X = O, (un)substituted NH; R1 = H, halo, CH2OH, alkyl, etc.; R2 = H, (un)substituted NHCO-aryl or alkyl] which are inhibitors of kinases useful as medications for treating various diseases, were prepared E.g., a multi-step synthesis of 5-bromo-4-[2-(1H-imidazol-4-yl)ethylamino]-2-(4-pyrrolidin-1-ylmethylphenylamino)pyrimidine, starting from 5-bromouracil, was given. Biol. data for inhibition of Akt-2, Chk-1, and VEGFR-II (KDR) were given. The pharmaceutical composition comprising the compds. I is claimed.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 6 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:777592 HCAPLUS
DOCUMENT NUMBER: 139:292270

TITLE: Substituted piperazine antithrombotic PAI-1 (plasminogen activator inhibitor-1) inhibitors, and their preparation, pharmaceutical compositions, and use in the treatment of thrombotic diseases.

INVENTOR(S): Chou, Yuo-Ling; Ghannam, Ameen; **Kochanny, Monica J.**; Lee, Wheeseong; Lu, Shou-Fu; Shaw, Kenneth J.; Ye, Bin; Zhao, Zuchun

PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany

SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

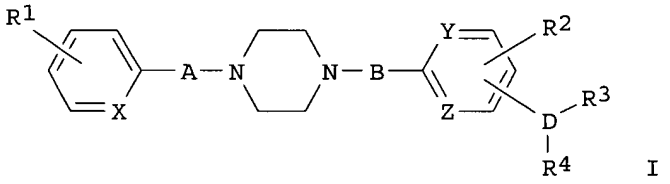
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003080060	A1	20031002	WO 2003-US7508	20030313

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

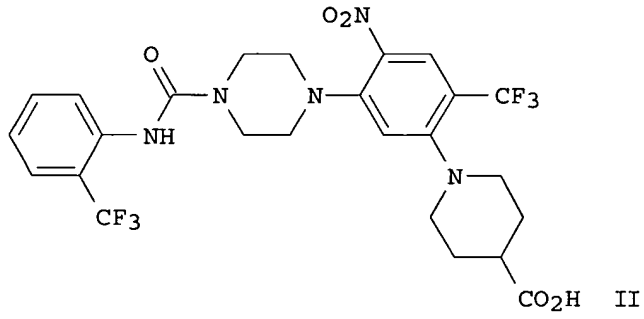
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-365988P P 20020320
OTHER SOURCE(S): MARPAT 139:292270

GI



I



II

AB The invention is directed to substituted piperazine compds. I and their pharmaceutically acceptable salts, which are useful as antithrombotic agents by inhibiting plasminogen activator inhibitor-1 (PAI-1) [wherein:

R1 = (one or more) H, haloalkyl, halo, or NO2; X, Y, Z = (independently) C or N; A = bond, CH2, CO, or alkylaminocarbonyl; B = bond, alkylaminocarbonyl, CH2, or carbonylalkylester (sic); R2 = halo, NO2, CO2H or alkyl ester, haloalkyl, dialkylamide, carboxamide, alkoxyaminocarbonyl, substituted aralkylamino, aryloxy, piperazinyl, imidazolyl, or pyridinyloxy, etc.; D = N or O; R3 = (un)substituted aryl, aralkyl, carboxycyclohexyl, carboxyalkyl, piperazinyl, alkoxy, aralkoxy, carboxypyrrolidinyl, carboxypiperidinyl, carboxypyridinyloxy, carboxypyridinyl; R4 = halo, NO2, CO2H, alkyl, alkyl ester, haloalkyl, menthyloxyalkylcarbonylamino, aralkylamino, etc.; or DR3R4 = atoms to form (un)substituted piperidine or pyrrolidine ring; or R2R3 = atoms to form dioxo-substituted heterocyclic group substituted by methylphosphonic acid (when Y = Z = C); including stereoisomers and/or pharmaceutically acceptable salts]. In addition, the invention relates to pharmaceutical compns., and methods of using the compds. to treat disease-states characterized by thrombotic activity. Over 100 compds. are listed, all of which inhibited human PAI-1 either in vitro (recombinant PAI-1 chromogenic hydrolysis assay), ex vivo (human plasma fibrin clot lysis assay), or both, with IC50 values of less than about 15 μM. Ten formulations of invention compound II are listed. Seven synthetic prepns. are described. For instance, 2,4-dichloro-5-nitrobenzotrifluoride was doubly aminated, first with N-BOC-piperazine in the 4-position, then with Et isonipecotate in the 2-position, followed by deprotection of the BOC-protected amine, carbamoylation of the amine with 2-(trifluoromethyl)phenyl isocyanate, and saponification of the ester with LiOH in aqueous THF, to give compound II.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 7 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:343927 HCAPLUS

DOCUMENT NUMBER: 139:332735

TITLE: Discovery and characterization of a potent and selective non-amidine inhibitor of human factor Xa

AUTHOR(S): Liang, Amy M.; Light, David R.; **Kochanny, Monica**; Rumennik, Galina; Trinh, Lan; Lentz, Dao; Post, Joseph; Morser, John; Snider, Michael

CORPORATE SOURCE: Berlex Biosciences, Richmond, CA, 94806-0099, USA

SOURCE: Biochemical Pharmacology (2003), 65(9), 1407-1418
CODEN: BCPCA6; ISSN: 0006-2952

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Benzothiophene-anthranilamide (3-chloro-N-[2-[[(4-fluorophenyl)amino]carbonyl]-4-methylphenyl]benzo[b]thiophene-2-carboxamide) was discovered by high throughput screening to be a highly potent and selective non-amidine inhibitor of human factor Xa with a Ki of 15 ± 4 nM. The compound is a selective inhibitor of human factor Xa as suggested by the Ki(app) determined for nine other human serine proteases and bovine trypsin. The activity of reconstituted human prothrombinase complex was inhibited by the compound when assayed in physiol. concns. of the substrate prothrombin. However, 27-fold higher inhibitor concns. were needed to achieve the same level of inhibition than were required for the inhibition of free factor Xa, due in part to non-specific binding of the inhibitor to phospholipid under the assay conditions. Failure to demonstrate enzymic cleavage of the compound suggests that it is solely an inhibitor rather than a substrate for factor Xa. The inhibition of factor Xa by the compound was reversible upon dilution of the enzyme/inhibitor mixture Analyses of the inhibition mechanism with Dixon, Cornish-Bowden, and Lineweaver-Burk plots showed that compound 1 is a linear mixed-type inhibitor with 5-fold higher affinity for free factor Xa than the factor

Xa/substrate complex. The linear mixed-type inhibition suggests that the compound binds to the active site region of factor Xa, but its binding cannot be fully displaced by the substrate S2222 (1 : 1 mixture of N-benzoyl-Ile-Glu-Gly-Arg-p-nitroanilide and N-benzoyl-Ile-Glu(γ-OMe)-Gly-Arg-p-nitroanilide hydrochloride). Thus, the inhibition mechanism for the compound is novel compared to most serine protease inhibitors including amidine-containing factor Xa inhibitors, which rely on binding to the S1 pocket of the enzyme active site. The compound represents an attractive, novel structural template for further development of efficacious, safe, and potentially orally active human factor Xa inhibitors.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 8 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:91228 HCAPLUS
DOCUMENT NUMBER: 139:62585
TITLE: Structure-Activity relationships of substituted benzothiophene-anthranilamide factor Xa inhibitors
AUTHOR(S): Chou, Yuo-Ling; Davey, David D.; Eagen, Keith A.; Griedel, Brian D.; Karanjawala, Rushad; Phillips, Gary B.; Sacchi, Karna L.; Shaw, Kenneth J.; Wu, Shung C.; Lentz, Dao; Liang, Amy M.; Trinh, Lan; Morrissey, Michael M.; **Kochanny, Monica J.**
CORPORATE SOURCE: Departments of Medicinal Chemistry and Molecular Pharmacology, Berlex Biosciences, Richmond, CA, 94804-0099, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(3), 507-511
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Compound 1 was identified by high throughput screening as a novel, potent, non-amidine factor Xa inhibitor with good selectivity against thrombin and trypsin. A series of modifications of the three aromatic groups of 1 was investigated. Substitution of chlorine or bromine for fluorine on the aniline ring led to the discovery of subnanomolar factor Xa inhibitors. Positions on the anthranilic acid ring that can accommodate further substitution were also identified.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 9 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:894400 HCAPLUS
DOCUMENT NUMBER: 138:133092
TITLE: Crystal Structures of Two Potent Nonamidine Inhibitors Bound to Factor Xa
AUTHOR(S): Adler, Marc; **Kochanny, Monica J.**; Ye, Bin; Rumennik, Galina; Light, David R.; Biancalana, Sara; Whitlow, Marc
CORPORATE SOURCE: Berlex Biosciences, Richmond, CA, 94804-0099, USA
SOURCE: Biochemistry (2002), 41(52), 15514-15523
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB There has been intense interest in the development of factor Xa inhibitors for the treatment of thrombotic diseases. Our laboratory has developed a series

of novel non-amidine inhibitors of factor Xa. This paper presents two crystal structures of compds. from this series bound to factor Xa. The first structure is derived from the complex formed between factor Xa and compound 1. Compound 1 was the first non-amidine factor Xa inhibitor from our laboratory that had measurable potency in an in vitro assay of anticoagulant activity. The second compound, 2, has a molar affinity for factor Xa (Kiapp) of 7 pM and good bioavailability. The two inhibitors bind in an L-shaped conformation with a chloroarom. ring buried deeply in the S1 pocket. The opposite end of these compds. contains a basic substituent that extends into the S4 binding site. A chlorinated Ph ring bridges the substituents in the S1 and S4 pockets via amide linkers. The overall conformation is similar to the previously published structures for amidine-based inhibitors complexed with factor Xa. However, there are significant differences in the interactions between the inhibitor and the protein at the atomic level. Most notably, there is no group that forms a salt bridge with the carboxylic acid at the base of the S1 pocket (Asp189). Each inhibitor forms only one well-defined hydrogen bond to the protein. There are no direct charge-charge interactions. The results indicate that electrostatic interactions play a secondary role in the binding of these potent inhibitors.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 10 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:89055 HCAPLUS

DOCUMENT NUMBER: 136:379473

TITLE: Design, Synthesis, and Biological Activity of Novel Factor Xa Inhibitors: 4-Aryloxy Substituents of 2,6-Diphenoxypyridines

AUTHOR(S): Ng, Howard P.; Buckman, Brad O.; Eagen, Keith A.; Guilford, William J.; **Kochanny, Monica J.**; Mohan, Raju; Shaw, Kenneth J.; Wu, Shung C.; Lentz, Dao; Liang, Amy; Trinh, Lan; Ho, Elena; Smith, David; Subramanyam, Babu; Vergona, Ron; Walters, Janette; White, Kathy A.; Sullivan, Mark E.; Morrissey, Michael M.; Phillips, Gary B.

CORPORATE SOURCE: Pharmaceuticals Research, Berlex Biosciences, Richmond, CA, 94804-0099, USA

SOURCE: Bioorganic & Medicinal Chemistry (2002), 10(3), 657-666
CODEN: BMECEP; ISSN: 0968-0896

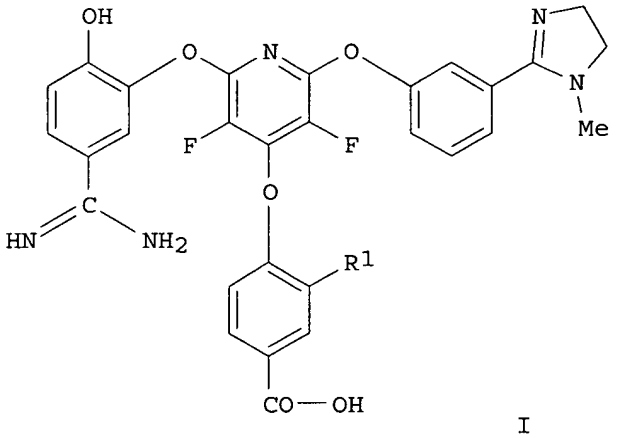
PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 136:379473

GI



I

AB A novel series of triaryloxypyridines have been designed to inhibit factor Xa, a serine protease strategically located in the coagulation cascade. Inhibitor 5e (I, R1 = OH) has a KI against factor Xa of 0.12 nM and is greater than 8000- and 2000-fold selective over two related serine proteases, thrombin and trypsin, resp. The 4-position of the central pyridine has been identified as a site that tolerates various substitutions without deleterious effects on potency and selectivity. This suggests that the 4-position of the pyridine ring is an ideal site for chemical modifications to identify inhibitors with improved pharmacokinetic characteristics. This investigation has resulted in inhibitor 5d (I, R1 = OCH3), which has an oral availability of 6% in dogs. The synthesis, in vitro activity, and in vivo profile of this class of inhibitors is outlined.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 11 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:202027 HCAPLUS

TITLE: Design, synthesis, and biological activity of novel non-amidine factor Xa inhibitors, 4: Optimization of hydrophilic substituents for potency and oral availability

AUTHOR(S): Ye, Bin; Cheeseman, Sarah; Chou, Yuo-Ling; Ewing, Janice; Fitch, Richard; Griedel, Brian D.; Karanjawala, Rushad; Lee, Wheeseong; Lentz, Dao; Liang, Amy; Morrissey, Michael M.; Post, Joseph; Sacchi, Karna L.; Sakata, Steven T.; Shaw, Kenneth J.; Subramanyam, Babu; Vergona, Ron; Walters, Janette; Wang, Yi-Xin; White, Kathy A.; Wu, Shung C.; Zhao, Zuchun; **Kochanny, Monica J.**

CORPORATE SOURCE: Berlex Biosciences, Richmond, CA, 94804-0099, USA

SOURCE: Abstracts of Papers, 221st ACS National Meeting, San Diego, CA, United States, April 1-5, 2001 (2001) MEDI-128
CODEN: 69FZD4

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal; Meeting Abstract

LANGUAGE: English

AB We have been investigating a series Factor Xa (fXa) inhibitors based on the thiophene-anthranilamide template I. In this poster, the optimization

of compds. for potency and bioavailability will be discussed. Incorporating a chloropyridine as the S1 binding element, and introducing a hydrophilic substituent on the central ring led to increased fXa and anticoagulant potency. Modification of the basic substituent on the thiophene afforded inhibitors with a wide range of potency and oral availability. This substituent was optimized to afford highly potent, orally available fXa inhibitors.

L84 ANSWER 12 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:202025 HCAPLUS
TITLE: Design, synthesis, and biological activity of novel non-amidine factor Xa inhibitors, 3: Replacement of the benzothiophene moiety with substituted thiophenes
AUTHOR(S): Lee, Wheeseong; Ewing, Janice; Griedel, Brian D.; Karanjawala, Rushad; Lentz, Dao; Liang, Amy; Morrissey, Michael M.; Post, Joseph; Sacchi, Karna L.; Sakata, Steven T.; Shaw, Kenneth J.; Ye, Bin; **Kochanny, Monica J.**
CORPORATE SOURCE: Berlex Biosciences, Richmond, CA, 94804-0099, USA
SOURCE: Abstracts of Papers, 221st ACS National Meeting, San Diego, CA, United States, April 1-5, 2001 (2001) MEDI-126
CODEN: 69FZD4
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; Meeting Abstract
LANGUAGE: English
AB We have been investigating a series Factor Xa (fXa) inhibitors based on the benzothiophene-anthranilamide template I. In the course of these studies, we found that the benzothiophene could be replaced by a suitably substituted thiophene (II). The resulting inhibitors had improved fXa potency and anticoagulant actvity. In this poster, the preparation and evaluation of compds. with benzylic heteroatom-containing substituents on the thiophene ring will be discussed. Generally, compds. with 3,4-disubstitution were more potent than compds. with 3,5-disubstitution.

L84 ANSWER 13 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:202022 HCAPLUS
TITLE: Design, synthesis, and biological activity of novel non-amidine factor Xa inhibitors, 2: Benzothiophene-anthranilamide analogs substituted on the central ring
AUTHOR(S): Chou, Yuo-Ling; Eagen, Keith A.; Griedel, Brian D.; Lentz, Dao; Liang, Amy; Morrissey, Michael M.; Shaw, Kenneth J.; Wu, Shung C.; **Kochanny, Monica J.**
CORPORATE SOURCE: Berlex Biosciences, Richmond, CA, 94804-0099, USA
SOURCE: Abstracts of Papers, 221st ACS National Meeting, San Diego, CA, United States, April 1-5, 2001 (2001) MEDI-123
CODEN: 69FZD4
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; Meeting Abstract
LANGUAGE: English
AB We have been investigating a series of Factor Xa (fXa) inhibitors based on the benzothiophene-anthranilamide template (I). In this poster, the preparation and evaluation of compds. with different substituents on the central anthranilamide ring will be discussed. Substitution with a halogen or Me group was strongly preferred at C-5, affording subnanomolar non-amidine inhibitors of fXa. Further investigation led to the identification of sites amenable to substitution for modification of physicochem. properties without loss of potency and selectivity.

L84 ANSWER 14 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:202018 HCAPLUS
TITLE: Design, synthesis, and biological activity of novel non-amidine Factor Xa inhibitors, 1: Structure-activity relationships of substituted benzothiophene-anthranilamides
AUTHOR(S): **Kochanny, Monica J.**; Davey, David D.; Eagen, Keith A.; Griedel, Brian D.; Karanjawala, Rushad; Lentz, Dao; Liang, Amy; Morrissey, Michael M.; Phillips, Gary B.; Sacchi, Karna L.; Snider, R. Michael; Trinh, Lan
CORPORATE SOURCE: Berlex Biosciences, Richmond, CA, 94804-0099, USA
SOURCE: Abstracts of Papers, 221st ACS National Meeting, San Diego, CA, United States, April 1-5, 2001 (2001) MEDI-120
CODEN: 69FZD4
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; Meeting Abstract
LANGUAGE: English
AB Our high throughput screening efforts led to the discovery of compound I as a novel non-amidine Factor Xa (fXa) inhibitor I (Ki=10 nM). We have been actively exploring the optimization of this template. This poster will discuss early SAR development around the fluorobenzene and benzothiophene portions of the template. This work led to fXa inhibitors with subnanomolar potency. In addition, efforts to introduce hydrophilic substituents for improvement of physicochem. properties will be presented.

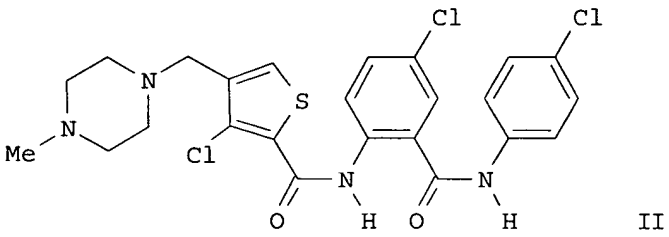
L84 ANSWER 15 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:201911 HCAPLUS
TITLE: Development of highly potent, selective, and orally available non-amidine factor Xa inhibitors
AUTHOR(S): **Kochanny, Monica J.**; Adler, Marc; Cheeseman, Sarah; Chou, Yuo-Ling; Davey, David D.; Eagen, Keith A.; Ewing, Janice; Fitch, Richard; Griedel, Brian D.; Karanjawala, Rushad; Lee, Wheeseong; Lentz, Dao; Liang, Amy; Morrissey, Michael M.; Phillips, Gary B.; Post, Joseph; Sacchi, Karna L.; Sakata, Steven T.; Shaw, Kenneth J.; Snider, R. Michael; Subramanyam, Babu; Trinh, Lan; Vergona, Ron; Walters, Janette; Wang, Yi-Xin; White, Kathy A.; Whitlow, Marc; Wu, Shung C.; Ye, Bin; Zhao, Zuchun
CORPORATE SOURCE: Berlex Biosciences, Richmond, CA, 94804-0099, USA
SOURCE: Abstracts of Papers, 221st ACS National Meeting, San Diego, CA, United States, April 1-5, 2001 (2001) MEDI-016
CODEN: 69FZD4
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; Meeting Abstract
LANGUAGE: English
AB Through high capacity screening, we identified the benzothiophene compound I as a novel non-amidine inhibitor of Factor Xa (fXa, Ki=10 nM). Although a potent fXa inhibitor, compound I had very poor anticoagulant activity in the prothrombin time assay and very poor solubility Efforts have been ongoing to optimize the potency and physicochem. properties of this template. The evolution of the lead compound into a series of highly potent, selective, and orally available inhibitors of fXa with submicromolar anticoagulant activity will be discussed.

L84 ANSWER 16 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:769086 HCAPLUS
DOCUMENT NUMBER: 133:335159
TITLE: Preparation of N-pyridinyl-2-[(thienylcarbonyl)amino]benzamides and analogs as anticoagulants
INVENTOR(S): Arnaiz, Damian O.; Chou, Yuo-ling; Griedel, Brian D.; Karanjawala, Rushad E.; **Kochanny, Monica J.**; Lee, Wheeseong; Liang, Amy Mei; Morrissey, Michael M.; Phillips, Gary B.; Sacchi, Karna Lyn; Sakata, Steven T.; Shaw, Kenneth J.; Snider, R. Michael; Wu, Shung C.; Ye, Bin; Zhao, Zuchun
PATENT ASSIGNEE(S): Berlex Laboratories, Inc., USA
SOURCE: U.S., 113 pp., Cont.-in-part of U.S. Ser. No. 994,284, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6140351	A	20001031	US 1998-187459	19981105
CA 2315070	AA	19990701	CA 1998-2315070	19981127
WO 9932477	A1	19990701	WO 1998-EP7650	19981127
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9918759	A1	19990712	AU 1999-18759	19981127
AU 751856	B2	20020829		
EP 1040108	A1	20001004	EP 1998-963519	19981127
EP 1040108	B1	20040225		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001526283	T2	20011218	JP 2000-525414	19981127
NZ 503809	A	20020426	NZ 1998-503809	19981127
AT 260103	E	20040315	AT 1998-963519	19981127
RU 2226529	C2	20040410	RU 2000-119756	19981127
PT 1040108	T	20040630	PT 1998-963519	19981127
ES 2215337	T3	20041001	ES 1998-963519	19981127
ZA 9811599	A	19990817	ZA 1998-11599	19981217
NO 2000003111	A	20000818	NO 2000-3111	20000616
US 6380221	B1	20020430	US 2000-631450	20000803
US 6498185	B1	20021224	US 2000-631452	20000803
PRIORITY APPLN. INFO.:			US 1997-994284 B2	19971219
			US 1998-187459 A	19981105
			WO 1998-EP7650 W	19981127

OTHER SOURCE(S): MARPAT 133:335159
GI



II

AB REZDR3 [I; D,E = Z1NR5C(:X), Z1NR5SO0-2, etc.; R,R3 = (un)substituted heterocyclyl or -aryl; R5 = H, (ar)alkyl, aryl; X = O, S, H2; Z = (un)substituted heterocyclylene or -arylene; Z1 = bond, alkylene, alkylidene, etc.] were prepared as factor Xa, thrombin, and prothrombinase inhibitors. Thus, H2NZCONHC6H4Cl-4 (Z = 4-chloro-1,2-phenylene)(preparation given) was N-acylated by 3-chloro-4-chloromethyl-2-thiophenecarbonyl chloride and the product aminated by 1-methylpiperazine to give title compound II. Data for biol. activity of I were given.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 17 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:818934 HCAPLUS

DOCUMENT NUMBER: 132:44977

TITLE: Benzamidine derivatives substituted by cyclic amino acid and cyclic hydroxy acid derivatives and their use as anticoagulants

INVENTOR(S): **Kochanny, Monica**; Morrissey, Michael M.; Ng, Howard P.

PATENT ASSIGNEE(S): Berlex Laboratories, Inc., USA

SOURCE: U.S., 31 pp., Cont.-in-part of U.S. Ser. No. 713,066.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6008234	A	19991228	US 1997-920319	19970827
CA 2264521	AA	19980319	CA 1997-2264521	19970911
WO 9811094	A1	19980319	WO 1997-EP4961	19970911
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9743843	A1	19980402	AU 1997-43843	19970911
AU 723999	B2	20000907		
EP 929547	A1	19990721	EP 1997-942015	19970911
EP 929547	B1	20021127		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CN 1234798	A	19991110	CN 1997-198664	19970911
JP 2001500147	T2	20010109	JP 1998-513257	19970911

JP 3565864	B2	20040915			
AT 228513	E	20021215	AT 1997-942015		19970911
PT 929547	T	20030331	PT 1997-942015		19970911
ES 2188979	T3	20030701	ES 1997-942015		19970911
KR 2000036017	A	20000626	KR 1999-701989		19990310
NO 9901206	A	19990511	NO 1999-1206		19990311
MX 9902396	A	20000331	MX 1999-2396		19990311
US 6177473	B1	20010123	US 1999-439065		19991112
US 6232325	B1	20010515	US 1999-438354		19991112
US 6265404	B1	20010724	US 1999-438270		19991112
CN 1338454	A	20020306	CN 2001-121736		20010703
PRIORITY APPLN. INFO.:			US 1996-713066	A2	19960912
			US 1997-920319	A	19970827
			WO 1997-EP4961	W	19970911

OTHER SOURCE(S): MARPAT 132:44977

AB Benzamidine derivs. substituted by cyclic amino acid and cyclic hydroxy acid derivs. are provided which are useful as anticoagulants. Also disclosed are pharmaceutical compns. containing the compds. of the invention, and methods of using the compds. to treat disease-states characterized by thrombotic activity.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 18 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:421679 HCAPLUS

DOCUMENT NUMBER: 131:87925

TITLE: Preparation of heteroarylcarbonylaminobenzamides and related compounds as anticoagulants.

INVENTOR(S): Arnaiz, Damian O.; Chou, Yuo-Ling; Karanjawala, Rushad E.; **Kochanny, Monica J.**; Lee, Wheeseong; Liang, Amy Mei; Morrissey, Michael M.; Phillips, Gary B.; Sacchi, Karna Lyn; Sakata, Stephen T.; Shaw, Kenneth J.; Snider, R. Michael; Wu, Shung C.; Ye, Bin; Zhao, Zuchun; Griedel, Brian D.

PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany

SOURCE: PCT Int. Appl., 326 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

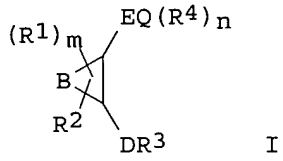
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9932477	A1	19990701	WO 1998-EP7650	19981127
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6140351	A	20001031	US 1998-187459	19981105
CA 2315070	AA	19990701	CA 1998-2315070	19981127
AU 9918759	A1	19990712	AU 1999-18759	19981127
AU 751856	B2	20020829		
EP 1040108	A1	20001004	EP 1998-963519	19981127
EP 1040108	B1	20040225		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, FI					
JP 2001526283	T2	20011218	JP 2000-525414		19981127
NZ 503809	A	20020426	NZ 1998-503809		19981127
AT 260103	E	20040315	AT 1998-963519		19981127
RU 2226529	C2	20040410	RU 2000-119756		19981127
NO 2000003111	A	20000818	NO 2000-3111		20000616
PRIORITY APPLN. INFO.:			US 1997-994284	A	19971219
			US 1998-187459	A	19981105
			WO 1998-EP7650	W	19981127

OTHER SOURCE(S): MARPAT 131:87925
GI



I

AB Title compds. [I; m = 1-3; n = 1-5; B, Q = atoms to form aryl, heterocyclyl rings; D, E = NR5CX; R8NR5CX, NR5SOp, etc.; p = 0-2; X = O, S, H2; R1 = H, alkyl, aryl, aralkyl, halo, haloalkyl, cyano, OR5, CO2R5, NR5R6, CONR5R6 (substituted) heterocyclyl, etc.; R2 = H, alkyl, aryl, aralkyl, halo, haloalkyl, cyano, OR5, CO2R5, CONR5R6, etc.; R3 = (substituted) heterocyclyl, aryl; R4 = H, alkyl, halo, haloalkyl, cyano, NO2, OR5, CO2R5, NR5R6, etc.; R5, R6 = H, alkyl, aryl, aralkyl; R8 = alkylene, alkenylene, alkynylene], were prepared Thus, N-(4-chlorophenyl)-2-[[(4-chloromethyl)-3-chlorothiophen-2-ylcarbonyl]amino]-3-methoxy-5-chlorobenzamide in DMF at 0° was treated with N-methylpiperazine followed by stirring to room temperature to give N-(4-chlorophenyl)-2-[[[4-[(4-methylpiperazin-1-yl)methyl]-3-chlorothiophen-2-yl]carbonyl]amino]-3-methoxy-5-chlorobenzamide. Title compds. routinely inhibited Factor Xa with Ki<3 nM. An aerosol formulation is given.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 19 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:487561 HCAPLUS
DOCUMENT NUMBER: 129:216581
TITLE: Design, synthesis, and evaluation of potential GAR and AICAR transformylase inhibitors
AUTHOR(S): Boger, Dale L.; **Kochanny, Monica J.**; Cai, Hui; Wyatt, Diane; Kitos, Paul A.; Warren, M. S.; Ramcharan, J.; Gooljarsingh, Lata T.; Benkovic, Stephen J.
CORPORATE SOURCE: Department of Chemistry, The Scripps Research Institute, La Jolla, CA, 92037, USA
SOURCE: Bioorganic & Medicinal Chemistry (1998), 6(6), 643-659
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Some derivs. of 5-(5-oxopentyl)pyrimidine-2,4-diamine were prepared and tested for the title activity. Some of the products showed reasonable activity against GAR transformylase.

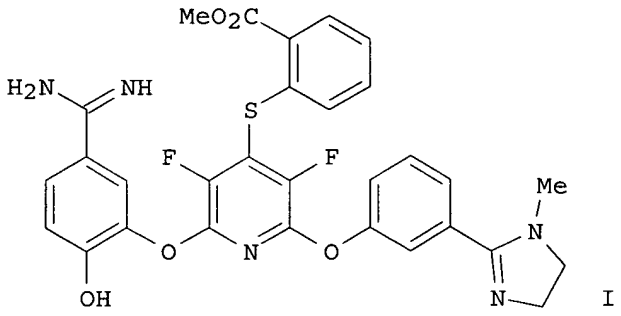
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 20 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:239218 HCAPLUS
DOCUMENT NUMBER: 128:294698
TITLE: Thio acid-derived monocyclic N-heterocyclics as anticoagulants
INVENTOR(S): **Kochanny, Monica J.**; Morrissey, Michael M.; Ng, Howard P.
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9815547	A1	19980416	WO 1997-EP5231	19970924
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6004985	A	19991221	US 1996-731128	19961009
CA 2268172	AA	19980416	CA 1997-2268172	19970924
AU 9746240	A1	19980505	AU 1997-46240	19970924
AU 730060	B2	20010222		
EP 934310	A1	19990811	EP 1997-944891	19970924
EP 934310	B1	20050209		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CN 1233247	A	19991027	CN 1997-198655	19970924
CN 1111159	B	20030611		
NZ 334758	A	20001124	NZ 1997-334758	19970924
JP 2001501632	T2	20010206	JP 1998-517127	19970924
AT 288908	E	20050215	AT 1997-944891	19970924
NO 9901594	A	19990608	NO 1999-1594	19990331
MX 9903294	A	20000228	MX 1999-3294	19990406
KR 2000048966	A	20000725	KR 1999-703014	19990408
US 6034084	A	20000307	US 1999-314619	19990519
US 6166014	A	20001226	US 1999-315120	19990519
US 6150382	A	20001121	US 1999-315790	19990521
HK 1020958	A1	20040227	HK 1999-106206	19991230
US 6162807	A	20001219	US 2000-481761	20000111
US 6221886	B1	20010424	US 2000-481987	20000111

PRIORITY APPLN. INFO.:
US 1996-731128 A 19961009
WO 1997-EP5231 W 19970924
US 1999-314619 A3 19990519

OTHER SOURCE(S): MARPAT 128:294698
GI



I

AB The invention is directed to a variety of monocyclic N-heterocyclics which are substituted by acyclic or cyclic thio derivs. The compds. are selective inhibitors of human factor Xa and thrombin, and are useful as anti-coagulants (no data). This invention is also directed to pharmaceutical compns. containing the compds., and methods of using them to treat thrombotic disease states. For instance, pentafluoropyridine underwent thioetherification in the 4-position using Me thiosalicylate (98%), etherification in the 2-position with 2-(benzyloxy)-5-cyanophenol (82%), etherification in the 6-position with 3-(1-methyl-2-imidazolin-2-yl)phenol (85%), and Pinner reaction of the nitrile function with concomitant debenzylation, to give title compound I, isolated as the CF3CO2H salt.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

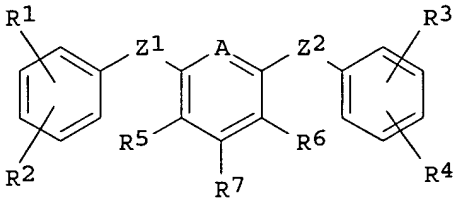
L84 ANSWER 21 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:180867 HCAPLUS
DOCUMENT NUMBER: 128:230376
TITLE: Benzamidine derivatives substituted by cyclic amino acid or cyclic hydroxy acid derivatives, and their use as anticoagulants
INVENTOR(S): **Kochanny, Monica**; Morrissey, Michael M.; Ng, Howard P.
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9811094	A1	19980319	WO 1997-EP4961	19970911
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6008234	A	19991228	US 1997-920319	19970827
CA 2264521	AA	19980319	CA 1997-2264521	19970911
AU 9743843	A1	19980402	AU 1997-43843	19970911

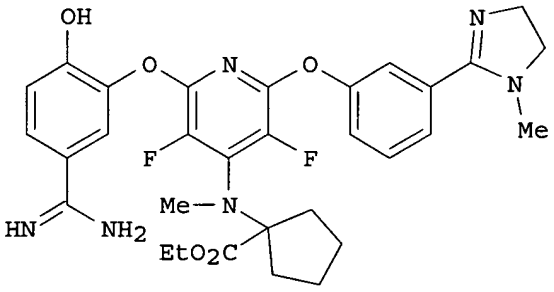
AU 723999	B2	20000907			
EP 929547	A1	19990721	EP 1997-942015		19970911
EP 929547	B1	20021127			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
JP 2001500147	T2	20010109	JP 1998-513257		19970911
JP 3565864	B2	20040915			
AT 228513	E	20021215	AT 1997-942015		19970911
NO 9901206	A	19990511	NO 1999-1206		19990311
MX 9902396	A	20000331	MX 1999-2396		19990311
PRIORITY APPLN. INFO.:			US 1996-713066	A	19960912
			US 1997-920319	A	19970827
			WO 1997-EP4961	W	19970911

OTHER SOURCE(S): MARPAT 128:230376

GI



I



II

AB The invention is directed to benzamidine derivs. substituted by cyclic amino acid and cyclic hydroxy acid derivs., which are represented by seven general formulas, e.g., I [A = CR8 or N; Z1, Z2 = O, NR9, S, S(O), S(O)2, or OCH2; R1, R4 = H, halo, alkyl, NO2, OR9, CO2R9, NR9R10 or derivs.; R2 = C(:NH)NH2, C(:NH)NHOR9, C(:NH)NHCO2R12, C(:NH)NHCOR9, etc.; R3 = H, alkyl, halo, haloalkyl, NO2, ureido, guanidino, OR9, C(:NH)NH2 or derivs., etc.; R5, R6 = H, halo, alkyl, haloalkyl, NR9R10, CO2R9, etc.; R7 = NR9(CR9R10)0-4R13, O(CR9R10)0-4R13, or NR14R15; R8 = H, alkyl, halo; R9, R10 = H, alkyl, (un)substituted aryl or aralkyl; R12 = alkyl, (un)substituted aryl or aralkyl; R13 = (un)substituted carbocycle; R13, NR14R15 = (un)substituted heterocycle]. The compds. are useful as anticoagulants. This invention is also directed to pharmaceutical compns. containing the compds., and their use to treat thrombotic disease states. For example, pentafluoropyridine underwent a sequence of: (1) amination in the 4-position by Et 1-amino-1-cyclopentanecarboxylate-HCl (82%); (2) N-methylation of the amino group (65%); (3) etherification in the 2-position with 2-(benzyloxy)-5-cyanophenol (60%); (4) etherification in

the 6-position with 3-(1-methylimidazolin-2-yl)phenol; and (5) Pinner reaction of the nitrile with concomitant debenzylation, to give title compound II (isolated as the CF3CO2H salt).

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 22 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:141230 HCAPLUS
TITLE: Development of potent, selective and orally available factor Xa inhibitors.
AUTHOR(S): Shaw, K. J.; Arnaiz, D. O.; Buckman, B. O.; Chou, Y. L.; Davey, D. D.; Eagen, K.; Griedel, B. D.; Guilford, W. J.; **Kochanny, M.**; Mohan, R.; Ng, H.; Phillips, G. B.; Pinkerton, M.; Sakata, S.; Wu, S. C.; Xu, W.; Yun, W.; Zhao, Z.; Light, D.; Dallas, J.; Koovakkat, S.; Whitlow, M.; Liang, A.; Trinh, L.; Ho, E.; Smith, D.; Subramanyam, B.; Vergona, R.; Walters, J.; White, K. A.; Sullivan, M. E.; Morrissey, M. M.
CORPORATE SOURCE: Berlex Biosciences, Richmond, CA, 94804, USA
SOURCE: Book of Abstracts, 215th ACS National Meeting, Dallas, March 29-April 2 (1998), MEDI-201. American Chemical Society: Washington, D. C.
CODEN: 65QTAA
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB Factor Xa (FXa) is a trypsin-like serine protease that plays a key role in the blood coagulation cascade. In our early studies we identified the active isomer of the published FXa inhibitor, 2,7-bis-(4-amidinobenzilidene)-cycloheptan-1-one (BABCH), as the (Z,Z) isomer (ZK-805412, FXa Ki = 0.66 nM). This isomer is derived from the photochem. isomerization of the (E,E) isomer. The (Z,Z) isomer has been used as a conformationally rigid template for the development of distinct classes of potent, selective and orally active FXa inhibitors. An overview of the in vitro and in vivo activities of these inhibitors will be presented.

L84 ANSWER 23 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:141155 HCAPLUS
TITLE: Design, synthesis and biological activity of novel factor Xa inhibitors. 5. Optimization of the C-4 position of the 2,6-diphenoxypyridine inhibitors for oral bioavailability.
AUTHOR(S): Davey, D. D.; Buckman, B. O.; Eagen, K.; Guilford, W. J.; **Kochanny, M.**; May, K. B.; Mohan, R.; Ng, H.; Phillips, G. B.; Pinkerton, M.; Shaw, K. J.; Wu, S. C.; Xu, W.; Yun, W.; Koovakkat, S.; Whitlow, M.; Liang, A.; Trinh, L.; Light, D.; Ho, E.; Smith, D.; Subramanyam, B.; Vergona, R.; Walters, J.; White, K. A.; Hinchman, J.; Post, J.; Sullivan, M. E.; Morrissey, M. M.
CORPORATE SOURCE: Berlex Biosciences, Richmond, CA, 94804, USA
SOURCE: Book of Abstracts, 215th ACS National Meeting, Dallas, March 29-April 2 (1998), MEDI-125. American Chemical Society: Washington, D. C.
CODEN: 65QTAA
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB A series of 4-amino and 4-alkoxy substituted 2,6-diphenoxypyridines was synthesized and the analogs evaluated for their ability to selectively inhibit factor Xa. Improvements in potency and oral bioavailability culminated in the discovery of ZK-807191. Synthesis, in vitro and in vivo

activity, as well as mol. modeling based on X-ray crystallog. expts., will be presented.

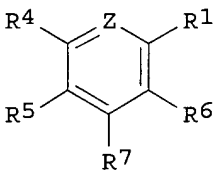
L84 ANSWER 24 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:141154 HCAPLUS
TITLE: Design, synthesis and biological activity of novel factor Xa inhibitors. 4. Aryloxy substitution at the C-4 position of the 2,6-diphenoxypyridine series.
AUTHOR(S): Ng, H. P.; Buckman, B. O.; Davey, D. D.; Eagen, K.; Guilford, W. J.; **Kochanny, M.**; Mohan, R.; Phillips, G. B.; Shaw, K. J.; Wu, S. C.; Xu, W.; Liang, A.; Trinh, L.; Ho, E.; Smith, D.; Subramanyam, B.; Vergona, R.; Walters, J.; White, K. A.; Sullivan, M. E.; Morrissey, M. M.
CORPORATE SOURCE: Berlex Biosciences, Richmond, CA, 94804, USA
SOURCE: Book of Abstracts, 215th ACS National Meeting, Dallas, March 29-April 2 (1998), MEDI-124. American Chemical Society: Washington, D. C.
CODEN: 65QTAA
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB The evolution of the bis-aryloxyamidine-based factor Xa inhibitors into potent 4-aryloxy substituted compds. (1) has been achieved. Prolonged plasma concns. are observed for these compds. in vivo as is selectivity for factor Xa over other serine proteases. The synthesis, in vitro activity and in vivo profile of this class of inhibitors will be described.

L84 ANSWER 25 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:542411 HCAPLUS
DOCUMENT NUMBER: 127:220575
TITLE: Preparation of pyridinyloxybenzamidines and analogs as factor Xa inhibitors
INVENTOR(S): **Kochanny, Monica**; Mohan, Raju; Morrissey, Michael M.; Ng, Howard P.; Yun, Weija
PATENT ASSIGNEE(S): Berlex Laboratories, Inc., USA
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

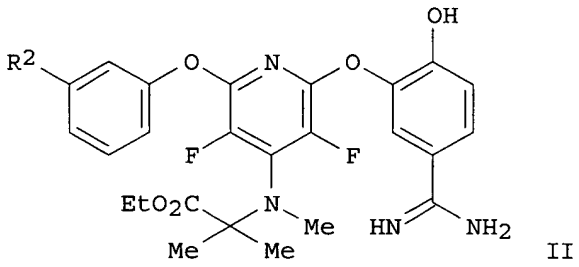
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9729067	A1	19970814	WO 1997-IB98	19970207
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5994375	A	19991130	US 1996-599834	19960212
CA 2245925	AA	19970814	CA 1997-2245925	19970207
AU 9714548	A1	19970828	AU 1997-14548	19970207
AU 715992	B2	20000217		
EP 888271	A1	19990107	EP 1997-901221	19970207
EP 888271	B1	20040428		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, LT, LV, FI				
CN 1211232	A	19990317	CN 1997-192215	19970207
NZ 326452	A	20000228	NZ 1997-326452	19970207

JP 2000505431	T2	20000509	JP 1997-528336		19970207
IL 125285	A1	20021110	IL 1997-125285		19970207
SK 283306	B6	20030502	SK 1998-1092		19970207
PL 186474	B1	20040130	PL 1997-328412		19970207
AT 265409	E	20040515	AT 1997-901221		19970207
PT 888271	T	20040930	PT 1997-901221		19970207
ES 2221032	T3	20041216	ES 1997-901221		19970207
ZA 9701183	A	19970918	ZA 1997-1183		19970212
NO 9803671	A	19980911	NO 1998-3671		19980811
NO 312834	B1	20020708			
US 6071912	A	20000606	US 1999-394458		19990909
US 6166088	A	20001226	US 1999-393180		19990909
US 6242454	B1	20010605	US 1999-393198		19990909
PRIORITY APPLN. INFO.:			US 1996-599834	A	19960212
			WO 1997-IB98	W	19970207

OTHER SOURCE(S): MARPAT 127:220575
GI



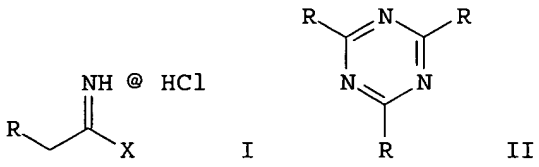
I



II

AB Title compds. [e.g., I; R1 = Z2Z3R3; R3 = (un)substituted amino, NHCONH2, C(:NH)NH2, heterocyclyl, etc.; R4 = Z1Z4R2; R2 = C(:NH)NHR; R = H, SO2R16, CONHR13, etc.; R5,R6 = H, halo, alkyl, (di)(alkyl)amino, etc.; R7 = NR9(CR10R11)nR12 or O(R10R11)mR12; R9 = H, (ar)alkyl, aryl, etc.; R10 = (cyclo)alkyl, aryl(alkyl), heterocyclyl(alkyl), etc.; R11 = H, (cyclo)alkyl, aryl; R12 = CO2R13 or CONR13R14; R13,R14 = H, (ar)alkyl, aryl, etc.; R16 = alkyl, aryl(alkyl), etc.; Z = CR8 or N; R8 = H, halo, alkyl; Z1,Z2 = O, NR13, S, OCH2; Z3,Z4 = (un)substituted phenylene; m = 1-6; n = 1-4] were prepared as factor Xa inhibitors (no data). Thus, pentafluoropyridine was aminated by H2NCMe2CO2Et and the N-methylated product etherified by 2-benzyloxy-5-cyanophenol to give, in 3 addnl. steps, title compd II [R2 = 1-methylimidazolin-2-yl (sic)].

L84 ANSWER 26 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:534077 HCAPLUS
DOCUMENT NUMBER: 121:134077
TITLE: Inverse Electron Demand Diels-Alder Reactions of Heterocyclic Azadienes: [4 + 2] Cycloaddition Reaction of Amidines with 1,3,5-Triazines
AUTHOR(S): Boger, Dale L.; **Kochanny, Monica J.**
CORPORATE SOURCE: Department of Chemistry, Scripps Research Institute, La Jolla, CA, 92037, USA
SOURCE: Journal of Organic Chemistry (1994), 59(17), 4950-5
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 121:134077
GI



I II

AB A detailed study of the scope of the amidine I (R = H, alkyl, etc.; X = NH2CH2CH2NH, etc.) Diels-Alder reaction with 1,3,5-triazines II (R = H, EtO2C, MeS) is described. The thermal reaction of amidines with sym. 1,3,5-triazines proceeds with in situ amidine to 1,1-diaminoethene tautomerization, [4+2] cycloaddn. with the 1,3,5-triazine, loss of ammonia from the initial Diels-Alder adduct with imine generation, imine to enamine tautomerization, and retro Diels-Alder loss of Et cyanoformate to provide substituted 4-aminopyrimidines in excellent conversions. The reaction proceeds best with the amidine hydrochloride salts at intermediate reaction temps. (90-100 °C) in polar, aprotic solvents, is rather invariant to the ratio of dienophile-diene used (1:2 equivalent 1:1 equivalent. 2:1), and is subject to triazine substituent effects characteristic of an inverse electron demand Diels-Alder reaction (R = CO2Et > R = H » R = SCH3). Notably, the generality of the amidine [4+2] cycloaddn. reaction with 1,3,5-triazines which was extended to include cyclic amidines effectively addresses the limitations of the alternative ynamine or N,O-ketene acetal dienophiles. A comparative examination of amidines, thioimidates, and imidates revealed that amidines are uniquely suited for use in this reaction cascade.

L84 ANSWER 27 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:430054 HCAPLUS
DOCUMENT NUMBER: 121:30054
TITLE: I. Fluorine-18 labeled corticosteroids and progestins for receptor-based imaging of the brain and of breast tumors. II. Synthesis and NMR spectrum of (13C18)-meso-hexestrol
AUTHOR(S): **Kochanny, Monica Jean**
CORPORATE SOURCE: Univ. Illinois, Urbana, IL, USA
SOURCE: (1993) 184 pp. Avail.: Univ. Microfilms Int., Order No. DA9314896
From: Diss. Abstr. Int. B 1993, 54(1), 247-8
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable

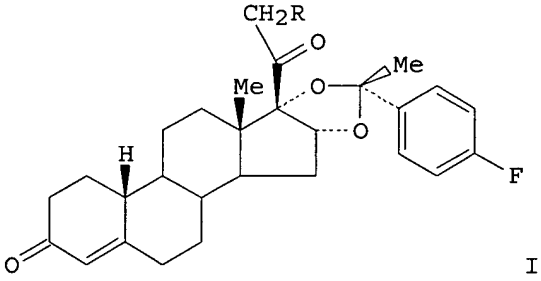
L84 ANSWER 28 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:96013 HCAPLUS
DOCUMENT NUMBER: 120:96013
TITLE: Synthesis and NMR spectrum of [13C18]-meso-hexestrol, a fully carbon-13 substituted ligand for NMR studies of the estrogen receptor
AUTHOR(S): **Kochanny, Monica J.**; Haerd, Torleif; Katzenellenbogen, John A.
CORPORATE SOURCE: Dep. Chem., Univ. Illinois, Urbana, IL, 61801, USA
SOURCE: Magnetic Resonance in Chemistry (1993), 31(11), 977-86
CODEN: MRCHEG; ISSN: 0749-1581
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The estrogen receptor ligand meso-hexestrol has been synthesized with 13C

enrichment (98 atomic%) at every position. 13C NMR spectra of the intermediates were obtained and 13C-13C coupling patterns analyzed. The complex 13C NMR spectrum of [13C18]-meso-hexestrol was simplified through the use of selective 13C decoupling. Several 13C-13C coupling consts. were estimated from the decoupled spectra and refined via iterative simulation. Some addnl. coupling consts. were measured in selective 1-dimensional 13C COSY spectra. Coupling consts. are reported to an accuracy of ±0.4-1 Hz. This study demonstrates the feasibility of determining 13C-13C coupling consts. in highly 13C-substituted compds.; such compds. are expected to be used with increased frequency in studying receptor-ligand interactions by polarization transfer methods.

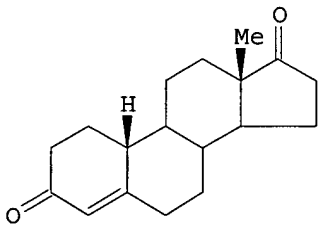
L84 ANSWER 29 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	1993:409029 HCAPLUS
DOCUMENT NUMBER:	119:9029
TITLE:	Fluorine-18 labeled progestin ketals: synthesis and target tissue uptake selectivity of potential imaging agents for receptor-positive breast tumors
AUTHOR(S):	**Kochanny, Monica J.**; VanBrocklin, Henry F.; Kym, Philip R.; Carlson, Kathryn E.; O'Neil, James P.; Bonasera, Thomas A.; Welch, Michael J.; Katzenellenbogen, John A.
CORPORATE SOURCE:	Dep. Chem., Univ. Illinois, Urbana, IL, 61801, USA
SOURCE:	Journal of Medicinal Chemistry (1993), 36(9), 1120-7 CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE:	Journal
LANGUAGE:	English
OTHER SOURCE(S):	CASREACT 119:9029

GI



I



II

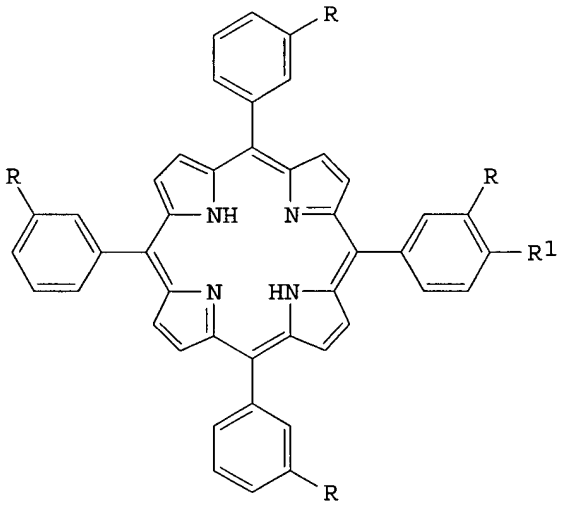
AB Two new fluorine-substituted progestins (I; R = H, OH) were studied as potential imaging agents for progesterone-receptor-pos. human breast tumors. The steroids are 16α,17α-fluoroacetophenone ketals of 16α,17α-dihydroxyprogesterone and 16α,17α,21-trihydroxy-19-norprogesterone. Synthesis of the latter compound in seven steps from 19-norandrost-4-ene-3,17-dione (II) is reported. Both compds. I demonstrate high affinity for the progesterone receptor (pgR) (52.5 and 240%, resp., relative to R5020 = 100). The syntheses were adapted to 18F-labeling with 4'-[18F]-fluoroacetophenone, prepared from 4'-nitroacetophenone by nucleophilic substitution with K18F/Kryptofix. Considerable adjustment of reaction conditions was required to effect ketalization using tracer quantities of the ketone. In tissue distribution studies in estrogen-primed immature female rats, both ketals showed selective uterine uptake, which was blocked by co-injection of a saturating dose of the unlabeled progestin ORG 2058. Addnl., metabolic stability of the radiolabel was indicated by the low radioactivity levels

seen in bone. Both compds. showed relatively high uptake in fat, in accord with their relative lipophilicities demonstrated by HPLC-derived octanol-water partition coeffs. The selective uterine uptake and metabolic stability of these compds. suggests that this class of PgR ligands might be promising for the selective imaging of receptor-pos. tumors if derivs. of reduced lipophilicity can be prepared

L84 ANSWER 30 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1993:229313 HCAPLUS
DOCUMENT NUMBER: 118:229313
TITLE: Fluorine-substituted corticosteroids: synthesis and evaluation as potential receptor-based imaging agents for positron emission tomography of the brain
AUTHOR(S): Pomper, Martin G.; **Kochanny, Monica J.**; Thieme, Andrea M.; Carlson, Kathryn E.; Vanbrocklin, Henry F.; Mathias, Carla J.; Welch, Michael J.; Katzenellenbogen, John A.
CORPORATE SOURCE: Dep. Chem., Univ. Illinois, Urbana, IL, 61801, USA
SOURCE: Nuclear Medicine and Biology (1992), 19(4), 461-80
CODEN: NMBIEO; ISSN: 0883-2897
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Eight fluorine-substituted corticosteroids representing ligands selective for Type I and Type II corticosteroid receptor subtypes as potential imaging agents for corticosteroid receptor-containing regions of the brain were prepared Receptor binding affinity assays show that fluorine substitution for hydroxyl or hydrogen in these steroids generally results in some reduction in affinity, with the result that the absolute affinity of these fluorine-substituted ligands for receptor is less than that typical for steroid hormones that show receptor-based, target selective uptake in vivo. Five of these compds. were prepared in fluorine-18 labeled form by a simple sulfonate ester displacement reaction, and their tissue distribution was studied in the adrenalectomized rat. There is no selective accumulation or selective retention of the Type I selective corticosteroids (18F-RU 2675, 21-[18F]fluoroprogesterone, 21-[18F]fluoro-11β-hydroxyprogesterone) in either the brain, or other target tissues (pituitary, kidney, liver). The Type II selective corticosteroids (18F-RU 28362, 18F-triamcinolone acetonide) show uptake into the hippocampus which can be partially blocked by a competing ligand; in target tissues outside the brain, the blocking is more complete. All of the 18F-labeled compds. show considerable defluorination, evident as high bone activity levels. These results, coupled with earlier findings in the literature, suggest that radiolabeled corticosteroid receptor ligands with both greater metabolic stability and higher receptor binding affinity and selectivity are needed for imaging corticosteroid receptors in the hippocampus.

L84 ANSWER 31 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1989:231312 HCAPLUS
DOCUMENT NUMBER: 110:231312
TITLE: Regiospecific aryl nitration of meso-substituted tetraarylporphyrins: a simple route to bifunctional porphyrins
AUTHOR(S): Kruper, William J., Jr.; Chamberlin, Thomas A.; **Kochanny, Monica**
CORPORATE SOURCE: Org. Chem. Polym. Lab., Dow Chem. USA, Midland, MI, 48674, USA
SOURCE: Journal of Organic Chemistry (1989), 54(11), 2753-6
CODEN: JOCEAH; ISSN: 0022-3263

DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 110:231312
GI



I

AB Mononitroaryltriarylporphyrins I (R = H, Me, OMe; R1 = NO2) were prepared by the direct nitration of I (R1 = H) with fuming nitric acid. Di- and trinitro derivs. were obtained only at higher HNO3 concns. I (R = H, R1 = NO2) was reduced to I (R = H, R1 = NH2) which was trisulfonated with H2SO4. The high selectivity and stepwise nature of the nitration has allowed for convenient preparation of porphyrins which can be covalently attached to polymers or macromols. of biol. interest.

```
=> => d stat que l86 nos
L66             STR
L68         601 SEA FILE=REGISTRY SSS FUL L66
L69             STR
L70          12 SEA FILE=REGISTRY SUB=L68 SSS FUL L69
L71           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L70
L72         589 SEA FILE=REGISTRY ABB=ON  PLU=ON  L68 NOT L70
L73         102 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L72
L74          86 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L73 AND PD=<OCTOBER 24, 2003
L75          86 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L74 NOT L71
L76          20 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L75 AND PATENT/DT
L77          66 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L75 NOT L76
L79          19 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("DUNNING L"/AU OR "DUNNING L
                A"/AU OR "DUNNING L K"/AU OR "DUNNING L KAY"/AU OR "DUNNING L
                L"/AU OR "DUNNING L M"/AU OR "DUNNING LAURA"/AU)
L80          18 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L79 NOT (L71 OR L76 OR L77)
L81          38 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("JAROCH S"/AU OR "JAROCH
                STEFAN"/AU)
L82          37 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L81 NOT (L71 OR L76 OR L77 OR
                L80)
L83          32 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("KOCHANNY M"/AU OR "KOCHANNY
                MONICA"/AU OR "KOCHANNY MONICA J"/AU OR "KOCHANNY MONICA
                JEAN"/AU)
L84          31 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L83 NOT (L71 OR L76 OR L77 OR
```

```
                L80 OR L82)
L85             5 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("LIAN X"/AU OR "LIAN X
                P"/AU) OR ("LIAN XIONG DONG"/AU OR "LIAN XIONGDONG"/AU)
L86             4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L85 NOT (L71 OR L76 OR L77 OR
                L80 OR L82 OR L84)


=> d ibib abs l86 1-4

L86  ANSWER 1 OF 4  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2004:288733  HCAPLUS
DOCUMENT NUMBER:          140:350343
TITLE:                    NO-1886 decreases ectopic lipid deposition and
                          protects pancreatic β cells in diet-induced
                          diabetic swine
AUTHOR(S):                Yin, W.; Liao, D.; Kusunoki, M.; Xi, S.; Tsutsumi, K.;
                          Wang, Z.; Lian, X.; Koike, T.; Fan, J.;
                          Yang, Y.; Tang, C.
CORPORATE SOURCE:         Department of Biochemistry and Biotechnology, Nanhua
                          University School of Life Sciences and Technology,
                          Hengyang, 421001, Peop. Rep. China
SOURCE:                   Journal of Endocrinology (2004), 180(3), 399-408
                          CODEN: JOENAK; ISSN: 0022-0795
PUBLISHER:                Society for Endocrinology
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB    The synthetic compound NO-1886 (ibrolipim) is a lipoprotein lipase activator
      that has been proven to be highly effective in lowering plasma
      triglycerides. Recently, we found that NO-1886 also reduced plasma free
      fatty acids and glucose in high-fat/high-sucrose diet-induced diabetic
      rabbits. In the current study, we investigated the effects of NO-1886
      treatment on ectopic lipid deposition and the islet pathol. in miniature
      swine fed a high-fat/high-sucrose diet. Our results showed that feeding
      this diet to miniature swine caused insulin resistance, increased lipid
      deposition in non-adipose tissue, such as in the heart, skeletal muscle,
      liver and pancreas, and also caused pancreatic β cell damage.
      However, supplementing 1% NO-1886 (200 mg/kg per day) into the
      high-fat/high-sucrose diet decreased ectopic lipid deposition, improved
      insulin resistance, and alleviated the β cell damage. These results
      suggest that improvement of lipid disorder, non-adipose tissue steatosis
      and insulin resistance may be very important for the protection of β
      cell damage. Therefore, NO-1886 is potentially beneficial for the
      treatment of insulin-resistance syndrome.
REFERENCE COUNT:          20    THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L86  ANSWER 2 OF 4  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2002:78983  HCAPLUS
DOCUMENT NUMBER:          136:408051
TITLE:                    Catalytic oxidation of methanol on molybdate-modified
                          platinum electrode in sulfuric acid solution
AUTHOR(S):                Li, W. S.; Tian, L. P.; Huang, Q. M.; Li, H.; Chen, H.
                          Y.; Lian, X. P.
CORPORATE SOURCE:         Department of Chemistry, South China Normal
                          University, Canton, 510631, Peop. Rep. China
SOURCE:                   Journal of Power Sources (2002), 104(2), 281-288
                          CODEN: JPSODZ; ISSN: 0378-7753
PUBLISHER:                Elsevier Science B.V.
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
```

AB The catalysis of methanol oxidation on molybdate-modified platinum was studied by using linear sweep voltammetry (LSV), cyclic voltammetry (CV) and chronoamperometry in the solns. with H2SO4 concns. from 0.5 to 4.5 M. It was found that methanol oxidation was catalyzed on the modified platinum by lowering methanol oxidation potential and promoting methanol oxidation current. There was the strongest catalysis in 3.7 M H2SO4 solution In this solution, methanol oxidation took place on the modified platinum at the potential 0.2 V more neg. than on the non-modified platinum and the steady oxidation current of methanol on the modified platinum at 0.7 V vs. SCE was 10 times that on the non-modified platinum. Molybdates were reduced to adsorbed hydrogen molybdenum(IV) bronzes on platinum in H2SO4 solution at a very neg. potential. The amount of reduced molybdates decreased with decreasing H2SO4 concns. The reduced molybdates were oxidized to different forms of hydrogen molybdenum bronzes (HxMoO3, 0<x<2) depending on the H2SO4 concentration Platinum was modified by these hydrogen molybdenum bronzes, but under-modified in the solution with lower H2SO4 concentration and over-modified in the solution with higher H2SO4 concentration The catalysis of methanol oxidation was weakened when the platinum was under- or over-modified.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L86 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:519116 HCAPLUS

DOCUMENT NUMBER: 133:281770

TITLE: [2]Catenane Assembly from Calix[4]arene Crown Ethers

AUTHOR(S): Li, Zhan-Ting; Zhang, Xiu-Lian; **Lian, Xiong-Dong**; Yu, Yi-Hua; Xia, Yi; Zhao, Cheng-Xue; Chen, Zhang; Lin, Zhi-Ping; Chen, Huan

CORPORATE SOURCE: Shanghai Institute of Organic Chemistry (SIOC), Chinese Academy of Sciences, Shanghai, 200032, Peop. Rep. China

SOURCE: Journal of Organic Chemistry (2000), 65(17), 5136-5142
CODEN: JOCEAH; ISSN: 0022-3263

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A variety of novel calix[4]arene-incorporating crown ethers with or without intramol. hydrogen bonding have been prepared by two efficient methods and utilized as donor rings to assemble calix[4]arene [2]catenanes based on π-stacking interaction between hydroquinone and bipyridinium units. Treatment of calix[4]arene crown ethers whose cone conformation was fixed by intramol. hydrogen bonding within the calix[4]arene moiety, with bis(bipyridiniummethyl)benzene 2PF6 salt and p-xylene dibromide afforded the corresponding [2]catenanes. Similar products were obtained with conformationally flexible calix[4]arenes having a cone conformation kept by two Pr groups. [2]Catenanes incorporating calix[4]arene in both the donor and acceptor rings were also successfully assembled from. The dynamic 1H NMR and absorption spectra of the [2]catenanes have been investigated, which revealed a strongest donor-acceptor interaction in the cone [2]catenanes and that the cone [2]catenanes can isomerize to the partial cone isomer at high temperature The difference of the dynamic properties of these catenanes was discussed. The results demonstrate that catenation is one new general method to change the conformational distributions of calix[4]arenes.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L86 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1990:212743 HCAPLUS

DOCUMENT NUMBER: 112:212743
TITLE: Spin-trapping studies of free radicals in human erythrocytes
AUTHOR(S): Hwang, F.; **Lian, X.**
CORPORATE SOURCE: Inst. Biophys., Acad. Sin., Beijing, Peop. Rep. China
SOURCE: Studia Biophysica (1989), 134(1-2), 105-10
CODEN: STBIBN; ISSN: 0081-6337
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The production of free radicals in erythrocyte membranes treated with cumene hydroperoxide hemin was demonstrated by the spin-trapping technique. The spin adduct of DMPO radical was observed by ESR, and its hyperfine splitting consts. were determined The production of free radicals can be inhibited by the adding of free radical scavengers. The possible mechanism of free radical formation initiated by the cumene hydroperoxide-hemin system is discussed.

=> => d stat que l89
L89 16 SEA FILE=HCAPLUS ABB=ON PLU=ON "LU SHOU FU"/AU

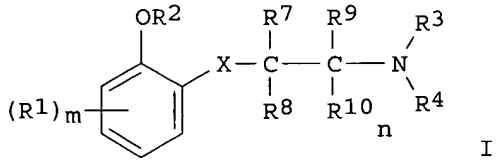
=> d ibib abs l89 1-16

L89 ANSWER 1 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:411067 HCAPLUS
DOCUMENT NUMBER: 142:463444
TITLE: Preparation of benzyl ether amine compounds useful as CCR-5 antagonists
INVENTOR(S): Davey, David; Lee, Wheeseong; **Lu, Shou-Fu**; Phillips, Gary; Wei, Guo Ping; Ye, Bin
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: U.S. Pat. Appl. Publ., 71 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005101644	A1	20050512	US 2004-984430	20041108
WO 2005047249	A1	20050526	WO 2004-US37258	20041108

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-519002P P 20031110
GI



I

AB The present invention relates to benzyl ether amines (shown as I; variables defined below; e.g. N-[[5-bromo-2-(4-chlorophenylmethoxy)phenyl]methyl]morpholineethanamine dihydrochloride (II)) that are CCR-5 receptor antagonists/. The invention further comprises pharmaceutical compns. comprising such compds., as well as the use of such compds. to treat CCR-5 mediated disorders. Antagonist compds. I were identified utilizing a CCR-5 receptor MIP1α SPA binding assay and exhibit IC50 values 0.01 μM-38 μM. For I: X is a bond or O; m = 0-4; n = 0-2; R1 = halogen, alkyl, haloalkyl, nitro, or -NR5R6; R2 is (a) H or (b) alkyl, cycloalkyl, alkenyl, aryl or heteroaryl any of which may be (un)substituted; R3 and R4 = (a) H; (b) alkyl, cycloalkyl, (cycloalkyl)alkyl, aryl, (aryl)alkyl, heterocyclo, (heterocyclo)alkyl, heteroaryl, or (heteroaryl)alkyl any of which may be (un)substituted with ≥1 Z1, Z2, Z3; or (c) -C(O)R*, -C(O)OR*, -C(O)NHR* or -SO2R*; or R3 and R4 together with the N atom to which they bonded may combine to form a heterocyclo or heteroaryl ring (un)substituted with ≥1 Z1, Z2, Z3. R7 and R8 = H, -OR10a, alkyl, hydroxyalkyl, or haloalkyl; or R7 and R8 may combine to form oxo; R9 and R10 = H, -OR10b, alkyl or haloalkyl; addnl. details are given in the claims. Although the methods of preparation are not claimed, .apprx.60 example prepns. are included. For example, II was prepared from 4-(2-aminoethyl)morpholine, 5-bromo-2-(4-chlorophenylmethyl)benzaldehyde and sodium triacetoxyborohydride in CH2Cl2.

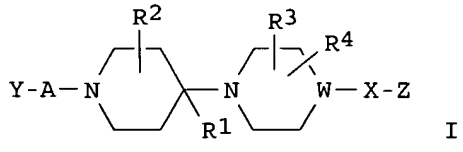
L89 ANSWER 2 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1154696 HCAPLUS
DOCUMENT NUMBER: 142:93694
TITLE: Preparation of quinolyl amide derivatives as CCR-5 antagonists
INVENTOR(S): **Lu, Shou-Fu**; Phillips, Gary; Ye, Bin
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004113323	A1	20041229	WO 2004-US18670	20040610

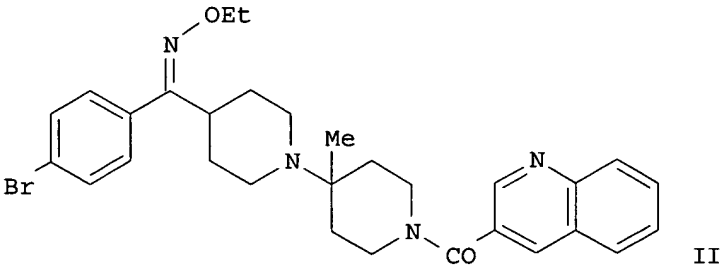
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,

SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2005020605 A1 20050127 US 2004-865976 20040610
PRIORITY APPLN. INFO.: US 2003-477940P P 20030613
OTHER SOURCE(S): MARPAT 142:93694
GI



I



II

AB Compds. of formula I [A = CO, SO2; W = N, CH; X = alkylene, CO, O, NH, etc.; Y = bicyclic heterocycle; Z = bromophenyl, trifluoromethylphenyl, fluorophenyl, pyridyloxy, etc.; R1-R4 = H, alkyl, alkenyl] are prepared which are CCR-5 receptor antagonists. Pharmaceutical compns. containing I are described. Thus, II was prepared from 3-quinolinecarboxylic acid and 4-[(4-bromophenyl)(ethoxyimino)methyl]-1-(4-methyl-4-piperidinyl)piperidine.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 3 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:51817 HCAPLUS
DOCUMENT NUMBER: 140:314423
TITLE: Synthesis and biological evaluation of piperazine-based derivatives as inhibitors of plasminogen activator inhibitor-1 (PAI-1)
AUTHOR(S): Ye, Bin; Chou, Yuo-Ling; Karanjawala, Rushad; Lee, Wheeseong; **Lu, Shou-Fu**; Shaw, Kenneth J.; Jones, Steven; Lentz, Dao; Liang, Amy; Tseng, Jih-Lie; Wu, Qingyu; Zhao, Zuchun
CORPORATE SOURCE: Berlex Biosciences, Discovery Research, Richmond, CA, 94804-0099, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(3), 761-765
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Compound I was identified by high throughput screening as a novel PAI-1 inhibitor. Systematic optimization of the A, B, and C segments of I resulted in the identification of a more potent compound II with good oral bioavailability. The synthesis and SAR data are presented in this report.
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 4 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:20661 HCAPLUS
DOCUMENT NUMBER: 140:93938
TITLE: Preparation of substituted quinolines useful as CCR5 receptor antagonists
INVENTOR(S): Dunning, Laura; Jaroch, Stefan; Kochanny, Monica J.; Lee, Wheeseong; Lian, Xiongdong; Liang, Meina; **Lu, Shou-Fu**; Onuffer, James; Phillips, Gary; Wei, Guo-Ping; Ye, Bin
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 241 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004002960	A1	20040108	WO 2003-US20950		20030624
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2489560	AA	20040108	CA 2003-2489560		20030624
BR 2003012204	A	20050426	BR 2003-12204		20030624
EP 1534681	A1	20050601	EP 2003-762325		20030624
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
US 2004072818	A1	20040415	US 2003-607530		20030626
PRIORITY APPLN. INFO.:			US 2002-451687P	P	20020627
			WO 2003-US20950	W	20030624

OTHER SOURCE(S): MARPAT 140:93938
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention relates to quinoline derivs. of formula I and II [wherein: R1, R1* = H, (un)substituted amino, alkyl, haloalkyl, OH, alkoxy, CO2R9a; R2, R2*, R3, R3* = H, (halo)alkyl, halogen, (un)substituted amino, nitro, cyano, alkoxy; R4, R4* = H, alkyl; R5 = H, R9, R9-aminocycloalk(en)yl, (alk/aryl)oxycarbonyl, SO2R9, C(O)NR7R9,

C(O)NR7-SO2R9, C(O)R6, C(O)R9, C(=NR10)R9, C(S)R9, C(=NR10)NHR9, C(S)NHR9, C(S)NR7-SO2R9; R6 is a group of formula III; R7, R7* = H, (un)substituted alkyl or aryl; R9a = arylalkyl, cycloalk(en)yl, cycloalkylalkyl, alkyl, heterocyclylalkyl, aryl, heterocyclyl any of which can be (un)substituted; R9 is same as R9a except H; R10 = H, cyano, (un)substituted alkyl or alkoxy; n = 0-3, n* = 1-3], their enantiomers, diastereomers, salts, and solvates. For instance, quinoline IV was prepared via amination of 4,7-dichloroquinoline by piperazine, and subsequent addition of obtained 7-chloro-4-(piperazin-1-yl)quinoline to 4-FC6H4NCO. The invention compds. are claimed as CCR5 receptor antagonists (no data) and useful for treating the CCR5-mediated inflammatory and immunoregulatory disorders such as optic neuritis, stroke, dermatitis, HIV, diabetes, etc.

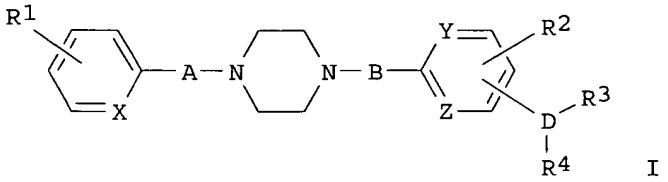
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 5 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:777592 HCAPLUS
DOCUMENT NUMBER: 139:292270
TITLE: Substituted piperazine antithrombotic PAI-1 (plasminogen activator inhibitor-1) inhibitors, and their preparation, pharmaceutical compositions, and use in the treatment of thrombotic diseases.
INVENTOR(S): Chou, Yuo-Ling; Ghannam, Ameen; Kochanny, Monica J.; Lee, Wheeseong; **Lu, Shou-Fu**; Shaw, Kenneth J.; Ye, Bin; Zhao, Zuchun
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

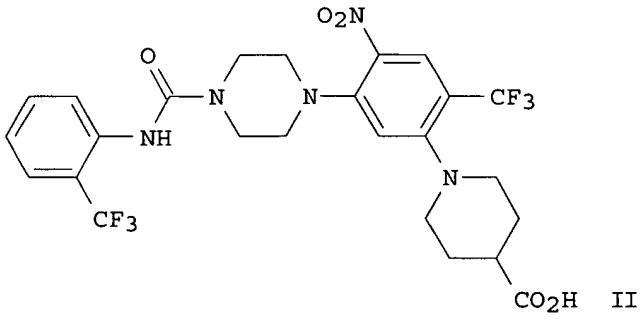
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003080060	A1	20031002	WO 2003-US7508	20030313

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-365988P P 20020320
OTHER SOURCE(S): MARPAT 139:292270
GI



I



II

AB The invention is directed to substituted piperazine compds. I and their pharmaceutically acceptable salts, which are useful as antithrombotic agents by inhibiting plasminogen activator inhibitor-1 (PAI-1) [wherein: R1 = (one or more) H, haloalkyl, halo, or NO2; X, Y, Z = (independently) C or N; A = bond, CH2, CO, or alkylaminocarbonyl; B = bond, alkylaminocarbonyl, CH2, or carbonylalkylester (sic); R2 = halo, NO2, CO2H or alkyl ester, haloalkyl, dialkylamide, carboxamide, alkoxyaminocarbonyl, substituted aralkylamino, aryloxy, piperazinyl, imidazolyl, or pyridinyloxy, etc.; D = N or O; R3 = (un)substituted aryl, aralkyl, carboxycyclohexyl, carboxyalkyl, piperazinyl, alkoxy, aralkoxy, carboxypyrrolidinyl, carboxypiperidinyl, carboxypyridinyloxy, carboxypyridinyl; R4 = halo, NO2, CO2H, alkyl, alkyl ester, haloalkyl, menthyloxyalkylcarbonylamino, aralkylamino, etc.; or DR3R4 = atoms to form (un)substituted piperidine or pyrrolidine ring; or R2R3 = atoms to form dioxo-substituted heterocyclic group substituted by methylphosphonic acid (when Y = Z = C); including stereoisomers and/or pharmaceutically acceptable salts]. In addition, the invention relates to pharmaceutical compns., and methods of using the compds. to treat disease-states characterized by thrombotic activity. Over 100 compds. are listed, all of which inhibited human PAI-1 either in vitro (recombinant PAI-1 chromogenic hydrolysis assay), ex vivo (human plasma fibrin clot lysis assay), or both, with IC50 values of less than about 15 μM. Ten formulations of invention compound II are listed. Seven synthetic prepns. are described. For instance, 2,4-dichloro-5-nitrobenzotrifluoride was doubly aminated, first with N-BOC-piperazine in the 4-position, then with Et isonipecotate in the 2-position, followed by deprotection of the BOC-protected amine, carbamoylation of the amine with 2-(trifluoromethyl)phenyl isocyanate, and saponification of the ester with LiOH in aqueous THF, to give compound II.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 6 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:211207 HCAPLUS
DOCUMENT NUMBER: 132:347443
TITLE: Syntheses of (R)- and (S)-2- and 6-

Fluoronorepinephrine and (R)- and (S)-2- and 6-Fluoroepinephrine: Effect of Stereochemistry on Fluorine-Induced Adrenergic Selectivities

AUTHOR(S): **Lu, Shou-fu**; Herbert, B.; Haufe, Guenter; Laue, Klaus Wilhelm; Padgett, William L.; Oshunleti, O.; Daly, John W.; Kirk, Kenneth L.

CORPORATE SOURCE: Laboratory of Bioorganic Chemistry National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, 20893, USA

SOURCE: Journal of Medicinal Chemistry (2000), 43(8), 1611-1619
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 132:347443

AB Several routes to the enantiomers of fluoronorepinephrines and fluoroepinephrines were explored. A catalytic enantioselective oxazaborolidine reduction and a chiral (salen)TiIV catalyzed asym. synthesis of silyl cyanohydrins proved efficacious in the key stereo-defining steps of two resp. routes. Binding studies of the catecholamines with α1-, α2-, β1-, and β2-adrenergic receptors were examined The assays confirmed that fluorine substitution had marked effects on the affinity of (R)-norepinephrine and (R)-epinephrine for adrenergic receptors, depending on the position of substitution. Thus, a fluoro substituent at the 2-position of (R)-norepinephrine and (R)-epinephrine reduced activity at both α1- and α2-receptors and enhanced activity at β1- and β2-receptors, while fluorination at the 6-position reduced activity at the β1- and β2-receptors. The effects of fluorine substitution on the S-isomers were less predictable.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 7 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:536462 HCAPLUS

DOCUMENT NUMBER: 131:283573

TITLE: Specificity of ascorbate analogs for ascorbate transport. Synthesis and detection of [125I]6-deoxy-6-iodo-L-ascorbic acid and characterization of its ascorbate-specific transport properties

AUTHOR(S): Rumsey, Steven C.; Welch, Richard W.; Garraffo, H. Martin; Ge, Ping; **Lu, Shou-Fu**; Crossman, Arthur T.; Kirk, Kenneth L.; Levine, Mark

CORPORATE SOURCE: Molecular and Clinical Nutrition Section, Digestive Diseases Branch, NIDDK, National Institutes of Health, Bethesda, MD, 20892-1372, USA

SOURCE: Journal of Biological Chemistry (1999), 274(33), 23215-23222
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Cellular ascorbic acid accumulation occurs in vitro by two distinct mechanisms: transport of ascorbate itself or transport and subsequent intracellular reduction of its oxidized product, dehydroascorbic acid. It is unclear which mechanism predominates in vivo. An easily detectable compound resembling ascorbate but not dehydroascorbic acid could be a powerful tool

to distinguish the two transport activities. To identify compds., 21 ascorbate analogs were tested for inhibition of ascorbate or dehydroascorbic acid transport in human fibroblasts. The most effective analogs, competitive inhibitors of ascorbate transport with Ki values of 3 μM, were 6-deoxy-6-bromo-, 6-deoxy-6-chloro-, and 6-deoxy-6-iodo-L-ascorbate. No analog inhibited dehydroascorbic acid transport. Using substitution chemical, [125I]6-deoxy-6-iodo-L-ascorbate (1.4+104 mCi/mmol) was synthesized. HPLC detection methods were developed for radiolabeled and nonradiolabeled compds., and transport kinetics of both compds. were characterized. Transport was sodium-dependent, inhibited by excess ascorbate, and similar to that of ascorbate. Transport of oxidized ascorbate and oxidized 6-deoxy-6-iodo-L-ascorbate was investigated using Xenopus laevis oocytes expressing glucose transporter isoform GLUT1 or GLUT3. Oxidation of ascorbate or its analog in media increased uptake of ascorbate in oocytes by 6-13-fold compared with control but not that of 6-deoxy-6-iodo-L-ascorbate. Therefore, 6-deoxy-6-iodo-L-ascorbate, although an effective inhibitor of ascorbate transport, either in its reduced or oxidized form was not a substrate for dehydroascorbic acid transport. Thus, radiolabeled and nonradiolabeled 6-deoxy-6-iodo-L-ascorbate provide a new means for discriminating dehydroascorbic acid and ascorbate transport in ascorbate recycling.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 8 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:267057 HCAPLUS
DOCUMENT NUMBER: 129:4794
TITLE: Synthesis of propyl O-(α-L-rhamnopyranosyl)-(1→3)-[2,4-di-O-(2s-methylbutyryl)-α-L-rhamnopyranosyl]-(1→2)-(3-O-acetyl-β-D-glucopyranosyl)-(1→2)-β-D-fucopyranoside, the tetrasaccharide moiety of Tricolorin A
AUTHOR(S): **Lu, Shou-Fu**; Ouyang, Qin-Qin; Guo, Zhong-Wu; Yu, Biao; Hui, Yong-Zheng
CORPORATE SOURCE: State Key Laboratory of Bio-organic and Natural Products Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai, 200032, Peop. Rep. China
SOURCE: Chinese Journal of Chemistry (1998), 16(1), 78-89
CODEN: CJOCEV; ISSN: 1001-604X
PUBLISHER: Science Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Pr O-(α-L-rhamnopyranosyl)-(1→3)-[2,4-di-O-(2s-methylbutyryl)-α-L-rhamnopyranosyl]-(1→2)-(3-O-acetyl-β-D-glucopyranosyl)-(1→2)-β-D-fucopyranoside, the tetrasaccharide moiety of Tricolorin A, was synthesized in a total of 23 steps with a longest linear sequence of 10 steps, and overall yield of 3.7% from D-glucose. The isomerization of the dioxolane-type benzylidene in the presence of NIS/AgOTf was observed The title tetrasaccharide exhibited no activity against the cultured P388 cell as Tricolorin A did.
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 9 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:66423 HCAPLUS
DOCUMENT NUMBER: 128:154298
TITLE: A novel and efficient deprotection of the allyl group at the anomeric oxygen of carbohydrates
AUTHOR(S): Yu, Biao; Zhang, Jian Bo; **Lu, Shou Fu**; Hui,

Yong Zheng
CORPORATE SOURCE: State Key Laboratory Bio-Organic Natural Products Chemistry, Shanghai Institute Organic Chemistry, Chinese Academy Sciences, Shanghai, 200032, Peop. Rep. China
SOURCE: Synlett (1998), (1), 29-30
CODEN: SYNLES; ISSN: 0936-5214
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 128:154298
AB Perfluoroalkylation with perfluoroalkyl iodide in the presence of Na2S2O4 and NaHCO3 in MeCN/H2O followed by elimination in the presence of Zn powder and NH4Cl in EtOH is an extremely mild and efficient procedure for deprotection of the anomeric allyl group of carbohydrates.

L89 ANSWER 10 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:18697 HCAPLUS
DOCUMENT NUMBER: 128:112825
TITLE: Recent progress on the research of resin glycosides
AUTHOR(S): **Lu, Shou-Fu**; Guo, Zhong-Wu; Ouyang, Qin-Qin; Hui, Yong-Zheng
CORPORATE SOURCE: State Key Lab. Bio-org. Nat. Prod. Chem., Shanghai Inst. Org. Chem., Chin. Acad. Sci., Shanghai, 200032, Peop. Rep. China
SOURCE: Youji Huaxue (1997), 17(6), 488-497
CODEN: YCHHDX; ISSN: 0253-2786
PUBLISHER: Kexue Chubanshe
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review with 24 refs. Recent studies on the structures, biol. activities, and chemical synthesis of resin glycosides in Convolvulaceae are summarized in this review.

L89 ANSWER 11 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:799287 HCAPLUS
DOCUMENT NUMBER: 128:61363
TITLE: An efficient one-step methyl esterification of carboxylic acid and deacetylation of alcohol under BF3·OEt2-MeOH
AUTHOR(S): **Lu, Shou Fu**; Ouyang, Qin Qin; Guo, Zhong Wu; Yu, Biao; Hui, Yong Zheng
CORPORATE SOURCE: State Key lab. Bioorg. nat. Prod. Chem., Shanghai Inst. Org. Chem., Acad. Sin., Shanghai, 200032, Peop. Rep. China
SOURCE: Chinese Chemical Letters (1997), 8(10), 843-844
CODEN: CCLEE7; ISSN: 1001-8417
PUBLISHER: Chinese Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An efficient of one-step Me esterification of carboxylic acid and deacetylation of alc. under BF3·OEt2-MeOH was developed.
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 12 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:799283 HCAPLUS
DOCUMENT NUMBER: 128:48418
TITLE: A new method for the cleavage of carbohydrate benzylidene acetal by ceric (IV) ammonium nitrate in

CH3CN-H2O (10:1)
AUTHOR(S): **Lu, Shou Fu**; Ouyang, Qin Qin; Guo, Zhong Wu; Yu, Biao; Hui, Yong Zheng
CORPORATE SOURCE: State Key Lab. Bio-org Nat. Prod. Chem., Shanghai Inst. Org. Chem., Acad. Sin., Shanghai, 200032, Peop. Rep. China
SOURCE: Chinese Chemical Letters (1997), 8(10), 841-842
CODEN: CCLEE7; ISSN: 1001-8417
PUBLISHER: Chinese Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A new method for the cleavage of carbohydrate benzylidene acetal has been developed using ceric(IV) ammonium nitrate (CAN) [(NH4)2Ce(NO3)6] in CH3CN-H2O (10/1, volume/volume).
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 13 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:766794 HCAPLUS
DOCUMENT NUMBER: 128:61707
TITLE: The first total synthesis of tricolorin A
AUTHOR(S): **Lu, Shou-Fu**; O'yang, QinQin; Guo, Zhong-Wu; Yu, Biao; Hui, Yong-Zheng
CORPORATE SOURCE: State Key Lab. Bio-organic Natural Products Chem., Shanghai Inst. Organic Chem., Chinese Academy Sciences, Shanghai, 200032, Peop. Rep. China
SOURCE: Angewandte Chemie, International Edition in English (1997), 36(21), 2344-2346
CODEN: ACIEAY; ISSN: 0570-0833
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Total preparation of tricolorin A from D-glucose is reported.
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 14 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:724057 HCAPLUS
DOCUMENT NUMBER: 127:331654
TITLE: Total Synthesis of Tricolorin A
AUTHOR(S): **Lu, Shou-Fu**; O'yang, QinQin; Guo, Zhong-Wu; Yu, Biao; Hui, Yong-Zheng
CORPORATE SOURCE: State Key Laboratory of Bio-organic and Natural Products Chemistry Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai, 200032, Peop. Rep. China
SOURCE: Journal of Organic Chemistry (1997), 62(24), 8400-8405
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

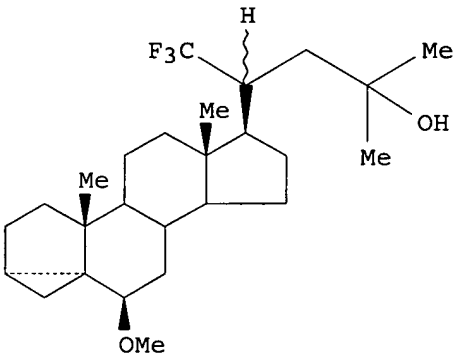
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Tricolorin A (I), a structurally amazing resin glycoside with promising bioactivities from Ipomoea tricolor cav. (convolvulaceae), was synthesized

in a total of 45 steps, with the longest linear sequence of 20 steps and overall yield of 0.65% from D-mannitol. The AB disaccharide 19-membered lactone was constructured by a regioselective macrolactonization using Corey-Nicolaou protocol. The macrolactone tetrasaccharide was realized either by "one-pot two-step" glycosylation procedure or by a stepwise assembly employing the "armed-disarmed" glycosylation strategy.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 15 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:226767 HCAPLUS
DOCUMENT NUMBER: 124:343791
TITLE: Synthesis of key intermediates to 20(R)- and 20(S)-trifluoromethyl-23,24-dinor-25-hydroxycholesterol and VD3 analogs
AUTHOR(S): **Lu, Shou-Fu**; Ruan, Ben-Fang; Wang, Zhong-Qo
CORPORATE SOURCE: Shanghai Inst. of Organic Chem., Chinese Academy of Sci., Shanghai, 200032, Peop. Rep. China
SOURCE: Chinese Journal of Chemistry (1996), 14(1), 60-6
CODEN: CJOCEV; ISSN: 1001-604X
PUBLISHER: Science Press
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB The key intermediates I to the title compds. were prepared from 3β-hydroxy-20-iodo-5,20-pregnadiene, using CF3SiMe3 as a trifluoromethylating agent.

L89 ANSWER 16 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:796279 HCAPLUS
DOCUMENT NUMBER: 123:314241
TITLE: An efficient synthesis and biological activities of 19-nor-17β-hydroxy-17α-trifluoromethyl-Δ4-estren-3-one and its analogs
AUTHOR(S): Wang, Zhong-Qi; **Lu, Shou-Fu**; Chao, Lin; Yang, Chuan-Jun
CORPORATE SOURCE: Shanghai Institute of Organic Chemistry, Chinese Academy of Science, Shanghai, 200032, Peop. Rep. China
SOURCE: Bioorganic & Medicinal Chemistry Letters (1995), 5(17), 1899-902
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier

DOCUMENT TYPE: Journal
LANGUAGE: English
AB 19-Nor-17β-hydroxy-17α-trifluoromethyl-Δ4-estren-3-one and its Δ4,9 and Δ4,9,11 analogs have been synthesized in total yields of 82%, 54% and 27%, resp., via trifluoromethylation of 19-nor-3,3-dimethoxy-Δ5(10)-estren-17-one using Me3SiCF3 as a trifluoromethylating agent. The three compds. showed high affinity for rat uterus progesterone receptor.

=> => d stat que l92 nos

```
L66             STR
L68         601 SEA FILE=REGISTRY SSS FUL L66
L69             STR
L70          12 SEA FILE=REGISTRY SUB=L68 SSS FUL L69
L71           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L70
L72         589 SEA FILE=REGISTRY ABB=ON  PLU=ON  L68 NOT L70
L73         102 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L72
L74          86 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L73 AND PD=<OCTOBER 24, 2003
L75          86 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L74 NOT L71
L76          20 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L75 AND PATENT/DT
L77          66 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L75 NOT L76
L79          19 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("DUNNING L"/AU OR "DUNNING L
                A"/AU OR "DUNNING L K"/AU OR "DUNNING L KAY"/AU OR "DUNNING L
                L"/AU OR "DUNNING L M"/AU OR "DUNNING LAURA"/AU)
L80          18 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L79 NOT (L71 OR L76 OR L77)
L81          38 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("JAROCH S"/AU OR "JAROCH
                STEFAN"/AU)
L82          37 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L81 NOT (L71 OR L76 OR L77 OR
                L80)
L83          32 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("KOCHANNY M"/AU OR "KOCHANNY
                MONICA"/AU OR "KOCHANNY MONICA J"/AU OR "KOCHANNY MONICA
                JEAN"/AU)
L84          31 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L83 NOT (L71 OR L76 OR L77 OR
                L80 OR L82)
L89          16 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "LU SHOU FU"/AU
L91          22 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("ONUFFER J"/AU OR "ONUFFER J
                J"/AU OR "ONUFFER JAMES"/AU OR "ONUFFER JAMES J"/AU OR
                "ONUFFER JAMES JOSEPH"/AU)
L92          20 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L91 NOT (L71 OR L76 OR L77 OR
                L80 OR L82 OR L84 OR L89)
```

=> d ibib abs l92 1-20

L92 ANSWER 1 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:739873 HCAPLUS
DOCUMENT NUMBER: 137:323811
TITLE: Chemokines, chemokine receptors and small-molecule antagonists: recent developments
AUTHOR(S): **Onuffer, James J.**; Horuk, Richard
CORPORATE SOURCE: Dept of Immunology, Berlex Biosciences, Richmond, CA, 94806, USA
SOURCE: Trends in Pharmacological Sciences (2002), 23(10), 459-467
CODEN: TPHSDY; ISSN: 0165-6147
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The physiol. roles of chemokine receptors have expanded beyond

host defense and now represent important targets for intervention in several disease indications. Chemokine receptors have joined the ranks of other members of the G-protein-coupled receptor (GPCR) family in therapeutic potential as small-mol. chemokine receptor antagonists move from discovery to the clinic. Chemokine receptors belong to the rhodopsin family of GPCRs and, as such, are expected to be closely related in structure to other Class A members. Here, the authors summarize information that is pertinent to chemokine receptors as therapeutic targets, the status of low mol. weight antagonists in clin. development, mol. modeling of receptor-small-mol. interactions, and the challenges that face drug discovery and development programs. Small-mol. antagonists of chemokine receptors (part of the G-protein-coupled receptor family) are likely to have valuable therapeutic roles in acute and chronic inflammation, angiogenesis and angiostasis, and as co-receptors for the cellular entry of HIV.

REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L92 ANSWER 2 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:74685 HCAPLUS

DOCUMENT NUMBER: 136:363556

TITLE: A chemokine receptor CCR-1 antagonist reduces renal fibrosis after unilateral ureter ligation

AUTHOR(S): Anders, Hans-Joachim; Vielhauer, Volker; Frink, Michael; Linde, Yvonne; Cohen, Clemens D.; Blattner, Simone M.; Kretzler, Matthias; Strutz, Frank; Mack, Matthias; Grone, Hermann-Josef; **Onuffer, James** ; Horuk, Richard; Nelson, Peter J.; Schlondorff, Detlef

CORPORATE SOURCE: Nephrological Center, Medizinische Poliklinik, Innenstadt, Universitat Munchen, Munchen, 80336, Germany

SOURCE: Journal of Clinical Investigation (2002), 109(2), 251-259
CODEN: JCINAO; ISSN: 0021-9738

PUBLISHER: American Society for Clinical Investigation

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The expression of chemokines and their receptors is thought to contribute to leukocyte infiltration and progressive renal fibrosis after unilateral ureter obstruction (UUO). We hypothesized that blocking the chemokine receptor CCR1 using the nonpeptide antagonist BX471 could reduce leukocyte infiltration and renal fibrosis after UUO. UUO kidneys from BX471-treated mice (day 0-10 and day 6-10) revealed a 40-60% reduction of interstitial macrophage and lymphocyte infiltrate compared with controls. Treated mice also showed a marked reduction of CCR1 and CCR5 mRNA levels, and FACS anal. showed a comparable reduction of CD8+/CCR5+ T cells. Markers of renal fibrosis, such as interstitial fibroblasts, interstitial volume, mRNA and protein expression for collagen I, were all significantly reduced by BX471-treatment compared with vehicle controls. By contrast treatment was ineffective when the drug was supplied only from days 0 to 5. In summary, blockade of CCR1 substantially reduces cell accumulation and renal fibrosis after UUO. Most interestingly, late onset of treatment is also effective. We therefore conclude that CCR1 blockade may represent a new therapeutic strategy for reducing cellular infiltration and renal fibrosis as major factors in the progression to end-stage renal failure.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L92 ANSWER 3 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:395022 HCAPLUS
DOCUMENT NUMBER: 135:118454
TITLE: Myomegalin is a novel protein of the Golgi/centrosome that interacts with a cyclic nucleotide phosphodiesterase
AUTHOR(S): Verde, Ignacio; Pahlke, Gudrun; Salanova, Michele; Zhang, Gu; Wang, Sonya; Coletti, Dario; **Onuffer, James**; Jin, S.-L. Catherine; Conti, Marco
CORPORATE SOURCE: Division of Reproductive Biology, Department of Gynecology and Obstetrics, Stanford University School of Medicine, Stanford, CA, 94305-5317, USA
SOURCE: Journal of Biological Chemistry (2001), 276(14), 11189-11198
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Subcellular targeting of the components of the cAMP-dependent pathway is thought to be essential for intracellular signaling. Here we have identified a novel protein, named myomegalin, that interacts with the cyclic nucleotide phosphodiesterase PDE4D, thereby targeting it to particulate structures. Myomegalin is a large 2,324-amino acid protein mostly composed of α-helical and coiled-coil structures, with domains shared with microtubule-associated proteins, and a leucine zipper identical to that found in the Drosophila centrosomin. Transcripts of 7.5-8 kilobases were present in most tissues, whereas a short mRNA of 2.4 kilobases was detected only in rat testis. A third splicing variant was expressed predominantly in rat heart. Antibodies against the deduced sequence recognized particulate myomegalin proteins of 62 kDa in testis and 230-250 kDa in heart and skeletal muscle. Immunocytochem. and transfection studies demonstrate colocalization of PDE4D and myomegalin in the Golgi/centrosomal area of cultured cells, and in sarcomeric structures of skeletal muscle. Myomegalin expressed in COS-7 cells coimmunopptd. with PDE4D3 and sequestered it to particulate structures. These findings indicate that myomegalin is a novel protein that functions as an anchor to localize components of the cAMP-dependent pathway to the Golgi/centrosomal region of the cell.
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L92 ANSWER 4 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:490314 HCAPLUS
DOCUMENT NUMBER: 133:247211
TITLE: The type IV phosphodiesterase specific inhibitor mesopram inhibits experimental autoimmune encephalomyelitis in rodents
AUTHOR(S): Dinter, H.; Tse, J.; Halks-Miller, M.; Asarnow, D.; **Onuffer, J.**; Faulds, D.; Mitrovic, B.; Kirsch, G.; Laurent, H.; Esperling, P.; Seidelmann, D.; Ottow, E.; Schneider, H.; Tuohy, V. K.; Wachtel, H.; Perez, H. D.
CORPORATE SOURCE: Department of Immunology, Berlex Biosciences, Richmond, CA, 94804, USA
SOURCE: Journal of Neuroimmunology (2000), 108(1-2), 136-146
CODEN: JNRIDW; ISSN: 0165-5728
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Exptl. autoimmune encephalomyelitis (EAE) is an autoimmune disease with

pathol. features reminiscent of those seen in multiple sclerosis and thus serves as an animal model for this disease. Inhibition of type IV phosphodiesterase (PDE IV) in animals with this disease has been shown to result in amelioration of disease symptoms. Here the authors describe the immunomodulatory activity of the novel potent and selective PDE IV inhibitor mesopram. In vitro, mesopram selectively inhibits the activity of type 1 helper T (Th1) cells without affecting cytokine production or proliferation of type 2 helper T (Th2) cells. Administration of mesopram to rodents inhibits EAE in various models. Clin., EAE is completely suppressed by mesopram in Lewis rats. This is accompanied by a reduction of inflammatory lesions in spinal cord and brain. RT-PCR anal. revealed a marked reduction in the expression of interferon-γ (IFN-γ) and tumor necrosis factor-α (TNF-α) in the brains of these animals. Furthermore, the ex vivo production of Th1 cytokines by activated spleen cells derived from mesopram-treated animals is significantly reduced compared to vehicle-treated controls. Amelioration of the clin. symptoms is also observed during chronic EAE in mesopram-treated SJL mice as well as in relapsing-remitting EAE in SWXJ mice using a therapeutic treatment regimen. These data demonstrate the anti-inflammatory activity of mesopram and provide a rationale for its clin. development.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L92 ANSWER 5 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:134477 HCAPLUS
DOCUMENT NUMBER: 127:75433
TITLE: Phosphodiesterase type IV inhibitors in the treatment of multiple sclerosis
AUTHOR(S): Dinter, Harald; **Onuffer, James**; Faulds, Daryl; Perez, H. Daniel
CORPORATE SOURCE: Department Immunology, Berlex Biosciences, Richmond, CA, 94804, USA
SOURCE: Journal of Molecular Medicine (Berlin) (1997), 75(2), 95-102
CODEN: JMLME8; ISSN: 0946-2716
PUBLISHER: Springer
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 70 refs. is given on phosphodiesterase type IV inhibitors and their potential application in the treatment of multiple sclerosis. Included is their effect on exptl. allergic encephalomyelitis and the regulation of phosphodiesterases type IV.

L92 ANSWER 6 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:398549 HCAPLUS
DOCUMENT NUMBER: 125:80142
TITLE: Tyrosine aminotransferase engineered from aspartate aminotransferase
AUTHOR(S): Malashkevich, Vladimir N.; **Onuffer, James**; Kirsch, Jack F.; Jansonius, Johan N.
CORPORATE SOURCE: Department Structural Biology, Biocenter the University Basel, Basel, CH-4056, Switz.
SOURCE: Perspectives on Protein Engineering & Complementary Technologies, Collected Papers, International Symposium, 3rd, Oxford, Sept. 13-17, 1994 (1995), Meeting Date 1994, 136-137. Editor(s): Geisow, Michael J.; Epton, Roger. Mayflower Worldwide: Kingswinford, UK.
CODEN: 62ZQAP
DOCUMENT TYPE: Conference

LANGUAGE: English
AB A hexamutant of Escherichia coli aspartate aminotransferase has been engineered, the kinetic properties of which closely approx. those of tyrosine aminotransferase, an enzyme with unusual bilateral substrate specificity. X-ray analyses of key inhibitor complexes of the mutant enzyme indicate that its almost equal affinity towards dicarboxylic and aromatic substrates is achieved by utilizing a common binding-site for both types of substrates, which specifically adapts to either type of side-chain. The current study represents an unusual example of effective regulation of substrate specificity via mutation of residues that do not formally belong to the substrate-binding site.

L92 ANSWER 7 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:860383 HCAPLUS
DOCUMENT NUMBER: 123:279656
TITLE: Redesign of the substrate specificity of Escherichia coli aspartate aminotransferase to that of Escherichia coli tyrosine aminotransferase by homology modeling and site-directed mutagenesis
AUTHOR(S): **Onuffer, James J.**; Kirsch, Jack F.
CORPORATE SOURCE: Dep. of Molecular and Cell Biology, Univ. of California, Berkeley, CA, 94720, USA
SOURCE: Protein Science (1995), 4(9), 1750-7
CODEN: PRCIEI; ISSN: 0961-8368
PUBLISHER: Cambridge University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Although several high-resolution x-ray crystallog. structures have been determined for Escherichia coli aspartate aminotransferase (eAATase), efforts to crystallize E. coli tyrosine aminotransferase (eTATase) have been unsuccessful. Sequence alignment analyses of eTATase and eAATase show 43% sequence identity and 72% sequence similarity, allowing for conservative substitutions. The high similarity of the two sequences indicates that both enzymes must have similar secondary and tertiary structures. Six active site residues of eAATase were targeted by homol. modeling as being important for aromatic amino acid reactivity with eTATase. Two of these positions (ZThr 109 and Asn 297) are invariant in all known aspartate aminotransferase enzymes, but differ in eTAT-ase (Ser 109 and Ser 297). The other four positions (Val 39, Lys 41, Thr 47, and Asn 69) line the active site pocket of eAATase and are replaced by amino acids with more hydrophobic side chains in eTATase (Leu 39, Tyr 41, Ile 47, and Leu 69). These six positions in eAATase were mutated by site-directed mutagenesis to the corresponding amino acids found in eTATase to redesign the substrate specificity of eAATase to that of eTATase. Five combinations of the individual mutations were obtained from mutagenesis reactions. The redesignated eAATase were mutated containing all six mutations (Hex) displays second-order rate consts. for the transamination of aspartate and phenylalanine that are within an order of magnitude of those observed for eTATase. Thus, the reactivity of eAATase with phenylalanine was increased by over three orders of magnitude without sacrificing the high transamination activity with aspartate observed for both enzymes. Examination of the dissociation consts. of the dicarboxylate inhibitor maleate and the aromatic inhibitor hydrocinnamate with the mutant constructs demonstrates that the T109S an N297S mutations are specific determinants for high-affinity association of nonpolar ligands, whereas the other four mutations have the general effect of decreasing the dissociation consts. for both dicarboxylate and nonpolar ligands. The latter four changes presumably exert their

general effect by stabilizing the closed conformation of the enzyme that is observed in x-ray crystals structures of eAATase complexes with dicarboxylate ligands.

L92 ANSWER 8 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:860382 HCAPLUS
DOCUMENT NUMBER: 123:279506
TITLE: The use of natural and unnatural amino acid substrates to define the substrate specificity differences of Escherichia coli aspartate and tyrosine aminotransferases
AUTHOR(S): **Onuffer, James J.**; Ton, Binh T.; Klement, Ivan; Kirsch, Jack F.
CORPORATE SOURCE: Dep. of Mol. and Cell Biology, Univ. of California, Berkeley, CA, 94720, USA
SOURCE: Protein Science (1995), 4(9), 1743-9
CODEN: PRCIEI; ISSN: 0961-8368
PUBLISHER: Cambridge University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The tyrosine (eTATase) and aspartate (eAATase) aminotransferases of Escherichia coli transaminate dicarboxylic amino acids with similar rate consts. However, eTATase exhibits .apprx. 102-104-fold higher second-order rate consts. for the transamination of aromatic amino acids than does eAATase. A series of natural and unnatural amino acid substrates was used to quantitate specificity differences for these two highly related enzymes. A general trend toward lower transamination activity with increasing side-chain length (extending from aspartate to glutamate to α-aminoadipate) is observed for both enzymes. This result suggests that dicarboxylate ligands associate with the two highly related enzymes in a similar manner. The high reactivity of the enzymes with L-Asp and L-Glu can be attributed to an ion pair interaction between the side-chain carboxylate of the amino acid substrate and the guanidino group of the active site residue Arg 292 that is common to both enzymes. A strong linear correlation between side-chain hydrophobicity and transamination rate consts. obtains for n-alkyl side-chain amino acid substrates with eTATase, but not for eAATase. The present kinetic data support a model in which eAATase contains one binding mode for all classes of substrate, whereas the active site of eTATase allows an addnl. mode that has increased affinity for hydrophobic amino acids.

L92 ANSWER 9 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:745007 HCAPLUS
DOCUMENT NUMBER: 123:221659
TITLE: Alternating arginine-modulated substrate specificity in an engineered tyrosine aminotransferase. [Erratum to document cited in CA123:106389]
AUTHOR(S): Malashkevich, Vladimir N.; **Onuffer, James J.**; Kirsch, Jack F.; Jansonius, Johan N.
CORPORATE SOURCE: Department of Structural Biology, University of Basel, Switz.
SOURCE: Nature Structural Biology (1995), 2(8), 704
CODEN: NSBIEW; ISSN: 1072-8368
PUBLISHER: Nature Publishing Co.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The errors were not reflected in the abstract or the index entries.

L92 ANSWER 10 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:679529 HCAPLUS

DOCUMENT NUMBER: 123:106389
TITLE: Alternating arginine-modulated substrate specificity in an engineered tyrosine aminotransferase
AUTHOR(S): Malashkevich, Vladimir N.; **Onuffer, James J.** ; Kirsch, Jack F.; Jansonius, Johan N.
CORPORATE SOURCE: Department of Structural Biology, University of Basel, Switz.
SOURCE: Nature Structural Biology (1995), 2(7), 548-53
CODEN: NSBIEW; ISSN: 1072-8368
PUBLISHER: Nature Publishing Co.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Mutation of six residues of Escherichia coli aspartate aminotransferase results in substantial acquisition of the transamination properties of tyrosine amino-transferase without loss of aspartate transaminase activity. X-ray crystallog. anal. of key inhibitor complexes of the hexamutant reveals the structural basis for this substrate selectivity. It appears that tyrosine aminotransferase achieves nearly equal affinities for a wide range of amino acids by an unusual conformational switch. An active-site arginine residue either shifts its position to electrostatically interact with charged substrates or moves aside to allow access of aromatic ligands.

L92 ANSWER 11 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:472981 HCAPLUS
DOCUMENT NUMBER: 123:78066
TITLE: Redesign of aspartate aminotransferase specificity to that of tyrosine aminotransferase
AUTHOR(S): Kirsch, Jack F.; **Onuffer, James J.**
CORPORATE SOURCE: Molecular and Cell Biology Department, University California, Berkeley, CA, 94720, USA
SOURCE: Biochem. Vitam. B6 PQQ, [Int. Meet. Vitam. B6 Carbonyl Catal.] (1994), 37-41. Editor(s): Marino, Gennaro; Sannia, Giovanni; Bossa, Francesco. Birkhaeuser: Basel, Switz.
CODEN: 60ZAAX
DOCUMENT TYPE: Conference
LANGUAGE: English
AB The values of kcat/Km are strongly correlated with chain length for the reactions of Escherichia coli tyrosine aminotransferase, but are nearly independent of this variable for aspartate aminotransferase. Both enzymes exhibit nearly equal reactivity with dicarboxylic acid substrates. Six key amino acid differences were identified that were found to be responsible for 80% of the specificity difference. It is postulated that a major role for Arg-292 in aspartate transaminase is to exclude nonspecific substrates by keeping the enzyme in an open inactive form. The free energy to close the enzyme into its active conformation derives from association with specific ligands.

L92 ANSWER 12 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:403791 HCAPLUS
DOCUMENT NUMBER: 121:3791
TITLE: Characterization of the apparent negative cooperativity induced in Escherichia coli aspartate aminotransferase by the replacement of Asp222 with alanine. Evidence for an extremely slow conformational change
AUTHOR(S): **Onuffer, James J.**; Kirsch, Jack F.
CORPORATE SOURCE: Dep. Mol. and Cell Biol., Univ. of California, Berkeley, CA, 94720, USA

SOURCE: Protein Engineering (1994), 7(3), 413-24
CODEN: PRENE9; ISSN: 0269-2139
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The strictly conserved active site residue, Asp222, which forms a hydrogen-bonded salt bridge with the pyridine nitrogen atom of the pyridoxal 5' phosphate (PLP) co-factor of aspartate aminotransferase (AATase), was replaced with alanine (D222A) in the Escherichia coli enzyme. The D222A mutant exhibits non-hyperbolic saturation behavior with amino acid substrates which appear as apparent neg. cooperativity in steady-state kinetic analyses. Single turnover progress curves for D222A are well described by the sum of two exponentials, contrasting with the monophasic kinetics of the wild-type enzyme. An active/inactive heterodimer containing the D222A mutation retains this biphasic kinetic response, proving that the observed cooperativity is not the result of induced allostery. The anomalous behavior is explained by a hysteretic kinetic model involving two slowly interconverting enzyme forms, only one of which is catalytically competent. The slow functional transition between the two forms has a half-life of .apprx.10 mins. Preincubation of the mutant with the dicarboxylic inhibitor maleate shifts the equilibrium population of the enzyme towards the catalytically active form, suggesting that the slow transition is related to the domain closure known to occur upon association of this inhibitor with the wild-type enzyme. The importance of Asp222 in the chemical steps of transamination is confirmed by the .apprx.105-fold decrease in catalytic competence in the D222A mutant, and by the large primary Cα-deuterium kinetic isotope effect (6.7 vs. 2.2 for the wild-type). The transamination activity of the D222A mutant is enhanced 4- to 20-fold by reconstitution with the co-factor analog N-methylpyridoxal-5'-phosphate (N-MePLP), and the Cα-proton abstraction step is less rate determining, as evidence by the decrease in the primary kinetic isotope effect from 6.7 to 2.3. These results suggest that the conserved interaction between the protonated pyridine nitrogen of PLP and the neg. charged carboxylate of Asp222 is important not only for efficient Cα-proton abstraction, but also for conformational transitions concomitant with the transamination process.

L92 ANSWER 13 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1992:647700 HCAPLUS
DOCUMENT NUMBER: 117:247700
TITLE: Characterization of tryptophan phosphorescence of aspartate aminotransferase from Escherichia coli
AUTHOR(S): Cioni, Patrizia; **Onuffer, James Joseph**; Strambini, Giovanni Battista
CORPORATE SOURCE: Ist. Biofis., Cent. Natl. Rech., Pisa, I-56127, Italy
SOURCE: European Journal of Biochemistry (1992), 209(2), 759-64
CODEN: EJBCAI; ISSN: 0014-2956
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The Trp phosphorescence spectrum, intensity and decay kinetics of apo-aspartate aminotransferase, pyridoxamine 5-phosphate (pyridoxamine 5P)-aspartate aminotransferase and pyridoxal 5P-aspartate aminotransferase were measured over a temperature range 160-273 K. The fine structure of the phosphorescence spectra in low-temperature glasses, with 0-0 vibrational bands centered at 408, 415 and 417 nm, for both apoenzyme and pyridoxamine 5P-enzyme reveals a marked heterogeneity of the chromophore environments. Only for the pyridoxal 5P form of the enzyme is the triplet emission strongly quenched and, in this case, the spectrum displays a unique 0-0 vibrational band centered at 415 nm. Concomitant to quenching, there is Trp-sensitized delayed fluorescence of the Schiff base, an indication that

quenching of the excited triplet state is due, at least in part, to a process of triplet singlet energy transfer to the keto-enamine tautomer. All three forms of the enzyme are phosphorescent for temps. up to 273 K. However, across the glass transition temperature the pyridoxal 5P enzyme shows a decrease in lifetime-normalized phosphorescence intensity, a thermal quenching that reduces even further the number of phosphorescing residues at ambient temperature In fluid solution, the triplet decay is nonexponential and multiple lifetimes stress the heterogeneity in dynamical structure of the chromophores' sites. For the pyridoxal-5P enzyme, where only one or at most two residues are phosphorescent at room temperature, the nonexponential nature of the decay implies the presence of different conformers of the protein not interconverting in the millisecond time scale.

L92 ANSWER 14 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1989:529731 HCAPLUS
DOCUMENT NUMBER: 111:129731
TITLE: Long-range electrostatic interactions can influence the folding, stability, and cooperativity of dihydrofolate reductase
AUTHOR(S): Perry, Kathleen M.; **Onuffer, James J.**; Gittelman, Mitchell S.; Barmat, Lawrence; Matthews, C. Robert
CORPORATE SOURCE: Dep. Biochem. Biophys., Univ. California, San Francisco, CA, 94143, USA
SOURCE: Biochemistry (1989), 28(19), 7961-8
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To test the possibility that long-range interactions might influence the folding and stability of Escherichia coli dihydrofolate reductase, a series of single and double mutations at positions 28 and 139 were constructed and their urea-induced unfolding reactions studied by absorbance and CD spectroscopy. The α-C atoms of the 2 side-chains were separated by 15 Å in the native conformation. The replacement of leucine-28 by arginine and of glutamate-139 by glutamine resulted in additive effects on both kinetic and equilibrium properties of the reversible unfolding transition; no evidence for interaction was obtained. In contrast, the arginine-28/lysine-139 double replacement changed the equilibrium folding model from 2-state to multistate and showed evidence for interaction in 1 of the 2 kinetic phases detected in both unfolding and refolding reactions. The results could be explained in terms of a long-range, repulsive electrostatic interaction between the cationic side-chains at these 2 positions.

L92 ANSWER 15 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:545193 HCAPLUS
DOCUMENT NUMBER: 109:145193
TITLE: The role of protein folding in the evolution of protein sequences
AUTHOR(S): Stackhouse, T.; **Onuffer, J. J.**; Matthews, C. R.; Ahmed, S. A.; Miles, E. W.
CORPORATE SOURCE: Dep. Chem., Pennsylvania State Univ., University Park, PA, 16802, USA
SOURCE: Cold Spring Harbor Symposia on Quantitative Biology (1987), 52(Evol. Catal. Funct.), 537-44
CODEN: CSHSAZ; ISSN: 0091-7451
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The folding and stability of the α-subunit of tryptophan synthase

from Escherichia coli, Salmonella typhimurium, and 5 interspecies hybrids produced by random combination of the structural genes for the parent proteins were examined In addition, 40 amino acid replacements were tested for their effects. Equilibrium and kinetic studies of folding showed that the parent and interspecies hybrid proteins all fold via the same rate-limiting steps and all involve ≥ 1 stable intermediate(s). This suggests conservation of the folding mechanism in the divergent evolution of these 2 organisms. Amino acid replacements in the region of residues 58-184 had little apparent effect on the stability and kinetics of folding. However, replacements in the N-terminal region (residues 1-58) play an important role in the stability of the protein.

L92 ANSWER 16 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:434487 HCAPLUS
DOCUMENT NUMBER: 109:34487
TITLE: Effects of the phenylalanine-22 → leucine, glutamic acid-49 → methionine, glycine-234 → aspartic acid and glycine-234 → lysine mutations on the folding and stability of the α subunit of tryptophan synthase from Escherichia coli [Erratum to document cited in CA104(23):203041c]
AUTHOR(S): Beasty, A. M.; Hurle, M. R.; Manz, J. T.; Stackhouse, T.; **Onuffer, J.**; Matthews, C. R.
CORPORATE SOURCE: Centocor, Malvern, PA, 19355, USA
SOURCE: Biochemistry (1988), 27(9), 3532
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The equation for Fapp has been corrected The error was not reflected in the abstract or the index entries.

L92 ANSWER 17 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:89645 HCAPLUS
DOCUMENT NUMBER: 108:89645
TITLE: Mutagenesis and protein folding
AUTHOR(S): Beasty, Anne M.; Chrunyk, Bris A.; Gittelman, Mitchell S.; Herndon, C. S.; Hurle, M. R.; Manz, J. T.; **Onuffer, J. J.**; Perry, K. M.; Stackhouse, T.; et al.
CORPORATE SOURCE: Dep. Chem., Pennsylvania State Univ., University Park, PA, 16802, USA
SOURCE: UCLA Symposia on Molecular and Cellular Biology, New Series (1987), 69(Protein Struct., Folding, Des. 2), 321-33
CODEN: USMBD6; ISSN: 0735-9543
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 12 refs. The replacement of individual amino acids in proteins (tryptophan synthetase, dihydrofolate reductase) may be used to demonstrate the participation of specific residues in limiting folding and stability.

L92 ANSWER 18 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:51996 HCAPLUS
DOCUMENT NUMBER: 108:51996
TITLE: Folding of homologous proteins: Conservation of the folding mechanism of the α subunit of tryptophan synthase from Escherichia coli, Salmonella typhimurium, and five interspecies hybrides
AUTHOR(S): Stackhouse, Thomas; **Onuffer, James J.**;

Matthews, C. Robert; Ahmed, Syed A.; Miles, Edith W.
CORPORATE SOURCE: Dep. Chem., Pennsylvania State Univ., University Park, PA, 16802, USA
SOURCE: Biochemistry (1988), 27(2), 824-32
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The equilibrium and kinetic properties for the urea-induced unfolding of the α subunit of tryptophan synthase from E. coli, S. typhimurium, and 5 interspecies hybrids were compared to determine the role of protein folding in evolution. The parent proteins differed at 40 positions in the sequence of 268 amino acids, and the hybrids differed by up to 15 amino acids from the E. coli α subunit. The results showed that all the proteins followed the same folding mechanism and were consistent with a previously proposed hypothesis that the folding mechanisms are conserved in homologous proteins. Anal. of the kinetic data suggested that the 15 positions at which the parent proteins differ in the amino folding unit, residues 1-188, do not play a role in a rate-limiting step in folding that has been previously identified as the association of the amino and carboxyl folding units. One or more of the 25 positions at which the parent proteins differ in the carboxyl folding unit, residues 189-268, do appear to play a role in this same rate-limiting step.

L92 ANSWER 19 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1987:191775 HCAPLUS
DOCUMENT NUMBER: 106:191775
TITLE: Effect of single amino acid replacements on the folding and stability of dihydrofolate reductase from Escherichia coli
AUTHOR(S): Perry, Kathleen M.; **Onuffer, James J.**; Touchette, Nancy A.; Herndon, Cinda S.; Gittelman, Mitchell S.; Matthews, Robert C.; Chen, Jin Tan; Mayer, Ruth J.; Taira, Kazunari; et al.
CORPORATE SOURCE: Dep. Chem., Pennsylvania State Univ., University Park, PA, 16802, USA
SOURCE: Biochemistry (1987), 26(10), 2674-82
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The role of the secondary structure in the folding mechanism of dihydrofolate reductase from E. coli was probed by studying the effects of amino acid replacements in 2 α-helixes and 2 strands of the central β-sheet on the folding and stability. The effects on stability could be qual. understood in terms of the x-ray structure for the wild-type protein by invoking electrostatic, hydrophobic, or H-bonding interactions. Kinetic studies focused on the 2 slow reactions that are thought to reflect the unfolding/refolding of 2 stable native conformers to/from their resp. folding intermediates. Replacements at 3 different positions in helix αB selectively altered the relaxation time for unfolding, whereas a single replacement in helix αC selectively altered the relaxation time for refolding. This behavior was characteristic of mutations that change the stability of the protein but do not affect the rate-limiting step. In striking contrast, replacements in strands βF and βG could affect both unfolding and refolding relaxation times. This behavior showed that these mutations alter the rate-limiting step in these native-to-intermediate folding reactions. It was proposed that the intermediates have an incorrectly formed β sheet whose maturation to the structure found in the native conformation is one of the slow steps in folding.

L92 ANSWER 20 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1986:203041 HCAPLUS
DOCUMENT NUMBER: 104:203041
TITLE: Effects of the phenylalanine-22 → leucine, glutamic acid-49 → methionine, glycine-234 → aspartic acid and glycine-234 → lysine mutations on the folding and stability of the α subunit of tryptophan synthase from Escherichia coli
AUTHOR(S): Beasty, A. M.; Hurle, M. R.; Manz, J. T.; Stackhouse, T.; **Onuffer, J. J.**; Matthews, C. R.
CORPORATE SOURCE: Centocor, Malvern, PA, 19355, USA
SOURCE: Biochemistry (1986), 25(10), 2965-74
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of 4 single amino acid replacements on the stability and folding of the α subunit of tryptophan synthase from E. coli were investigated by UV difference spectroscopy. In previous studies, the urea-induced unfolding at pH 7.8, 25°, was shown to proceed by the initial unfolding of the less stable C-terminal domain (residues 189-268) followed by the unfolding of the more stable N-terminal domain (residues 1-188). The effects of the phenylalanine (Phe)-22 → leucine (Leu)-22, glutamate (Glu)-49 → methionine (Met)-49, glycine (Gly)-234 → aspartate (Asp)-234, and Gly-234 → lysine (Lys)-234 mutations on the equilibrium unfolding process could all be understood in terms of the domain-unfolding model. With the exception of the Glu-49 → Met-49 replacement, the effects on stability were small. In contrast, the effects of 3 of the 4 mutations on the kinetics of interconversion of the native form and 1 of the stable partially folded intermediates were dramatic. The results for the Phe-22 → Leu-22 and Gly-234 → Asp-234 mutations indicated that these residues play a key role in the rate-limiting step. The Glu-49 → Met-49 mutation increased the stability of the native form with respect to that of the intermediate but did not affect the rate-limiting step. The Gly-234 → Lys-234 mutation did not affect either the stability or the kinetics of folding for the transition between native and intermediate forms. The changes in stability calculated from the unfolding and refolding rate consts. agreed quant. with those obtained from the equilibrium data. Consideration of these results and those from a previous study on the Gly-211 → Glu-211 replacement indicated that the rate-limiting step in the conversion of the intermediate to the native conformation involves either domain association or some other type of mol.-wide phenomenon.

=> => d stat que l95 nos
L66 STR
L68 601 SEA FILE=REGISTRY SSS FUL L66
L69 STR
L70 12 SEA FILE=REGISTRY SUB=L68 SSS FUL L69
L71 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L70
L72 589 SEA FILE=REGISTRY ABB=ON PLU=ON L68 NOT L70
L73 102 SEA FILE=HCAPLUS ABB=ON PLU=ON L72
L74 86 SEA FILE=HCAPLUS ABB=ON PLU=ON L73 AND PD=<OCTOBER 24, 2003
L75 86 SEA FILE=HCAPLUS ABB=ON PLU=ON L74 NOT L71
L76 20 SEA FILE=HCAPLUS ABB=ON PLU=ON L75 AND PATENT/DT
L77 66 SEA FILE=HCAPLUS ABB=ON PLU=ON L75 NOT L76
L79 19 SEA FILE=HCAPLUS ABB=ON PLU=ON ("DUNNING L"/AU OR "DUNNING L A"/AU OR "DUNNING L K"/AU OR "DUNNING L KAY"/AU OR "DUNNING L L"/AU OR "DUNNING L M"/AU OR "DUNNING LAURA"/AU)
L80 18 SEA FILE=HCAPLUS ABB=ON PLU=ON L79 NOT (L71 OR L76 OR L77)

```
L81          38 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("JAROCH S"/AU OR "JAROCH
                STEFAN"/AU)
L82          37 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L81 NOT (L71 OR L76 OR L77 OR
                L80)
L83          32 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("KOCHANNY M"/AU OR "KOCHANNY
                MONICA"/AU OR "KOCHANNY MONICA J"/AU OR "KOCHANNY MONICA
                JEAN"/AU)
L84          31 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L83 NOT (L71 OR L76 OR L77 OR
                L80 OR L82)
L89          16 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "LU SHOU FU"/AU
L91          22 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("ONUFFER J"/AU OR "ONUFFER J
                J"/AU OR "ONUFFER JAMES"/AU OR "ONUFFER JAMES J"/AU OR
                "ONUFFER JAMES JOSEPH"/AU)
L92          20 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L91 NOT (L71 OR L76 OR L77 OR
                L80 OR L82 OR L84 OR L89)
L94          62 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "WEI GUO"/AU OR ("WEI GUO
                PIN"/AU OR "WEI GUO PING"/AU)
L95          56 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L94 NOT (L71 OR L76 OR L77 OR
                L80 OR L82 OR L84 OR L89 OR L92)


=> d ibib abs l95 1-56

L95  ANSWER 1 OF 56  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:        2005:920899  HCAPLUS
TITLE:                   Protective effect and mechanism of mastoparan-1 on
                         septic mice
AUTHOR(S):               Guo, Yibin; Zheng, Jiang; Lu, Genfa; Wei, Guo
CORPORATE SOURCE:        Southwest Hospital, Third Military Medical University,
                         Chongqing, 400038, Peop. Rep. China
SOURCE:                  Zhonghua Chuangshang Zazhi (2004), 20(11), 678-681
                         CODEN: ZCZAFD; ISSN: 1001-8050
PUBLISHER:               Zhonghua Chuangshang Zazhi Bianjibu
DOCUMENT TYPE:           Journal
LANGUAGE:                Chinese
AB   The influence of cationic peptide mastoparan-1 (MP-1) on respiratory burst
     of murine peritoneal macrophages (PMφ) stimulated by
     lipopolysaccharide (LPS) was studied.  The protecting effect of MP-1 (3
     mg/kg) on mice challenged by lethal LPS (20 mg/kg) was observed by means that
     the murine PMφ was preincubated with MP-1 for two hours in vitro
     before the murine PMφ was stimulated with LPS (400 ng/mL).  The
     superoxide anion and the activity of NADPH oxidase in PMφ were assayed
     by fluorescence spectrophotometry and the hydrogen peroxide released from
     PMφ measured by UV spectrophotometry.  MP-1 could significantly
     protect mice from LPS challenging and inhibit the value of superoxide
     anion and hydrogen peroxide as well as the activity of NADPH oxidase in
     PMφ.  MP-1 could exert significantly protective effect on the mice
     challenged by lethal LPS, which might be related to the inhibitive effect
     of MP-1 on the respiratory burst in macrophage of the septic mice.

L95  ANSWER 2 OF 56  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:        2005:882920  HCAPLUS
TITLE:                   Health preparation for skin care
INVENTOR(S):             Junfeng,  Song; Wei,  Guo
PATENT ASSIGNEE(S):      Xibei Univ., Peop. Rep. China
SOURCE:                  Faming Zhuanli Shenqing Gongkai Shuomingshu, No pp.
                         given
                         CODEN: CNXXEV
DOCUMENT TYPE:           Patent
LANGUAGE:                Chinese
```

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1088086	A	19940622	CN 1992-114587	19921214

PRIORITY APPLN. INFO.: CN 1992-114587 19921214
AB Unavailable

L95 ANSWER 3 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:693331 HCAPLUS
TITLE: The function of the SNP in the MMP1 and MMP3 promoter in susceptibility to endometriosis in China
AUTHOR(S): Shan, Kang; Wang, Ying; Zhang, Jian-Hui; **Wei, Guo**; Wang, Na; Yan, Li
CORPORATE SOURCE: Department of Obstetrics and Gynaecology, Fourth Hospital, Hebei Cancer Institute, Hebei Medical University, Shijiazhuang, Peop. Rep. China
SOURCE: Molecular Human Reproduction (2005), 11(6), 423-427
CODEN: MHREFD; ISSN: 1360-9947
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Matrix metalloproteinases (MMPs) may contribute to the development of endometriosis. Genetic variations in several MMP promoters may influence the transcription and expression of MMPs. The purpose of the present study was to assess how gene polymorphisms in the MMP1 and MMP3 promoters affect the risk of development of endometriosis. We genotyped 100 women with endometriosis and 150 control subjects in North China. There was a significant difference in frequency of the MMP1 genotype between cases and controls ($P = 0.03$). The 2G homozygote in endometriosis and controls was significantly different ($P = 0.02$). The frequency of the 2G allele among affected women (79%) was significantly higher than among the healthy controls (66.9%; $P = 0.003$). However, the overall genotype and allelotype distribution of the MMP3 single nucleotide polymorphism (SNP) in patients was not different from that of controls ($P \geq 0.05$). MMP1 and MMP3 polymorphisms were in linkage disequil. in cases and controls ($D' = 0.47$; $P = 0.00$). The haplotype frequency distribution derived from these two polymorphisms was significantly different between cases and controls ($P = 0.00$). The haplotype anal. suggested an implication of both MMP1 and MMP3 polymorphisms in the susceptibility to endometriosis. We conclude that the MMP1 promoter SNP and MMP 2G/6A haplotype may modify susceptibility to endometriosis, but that the MMP3 promoter SNP is unlikely to be associated with endometriosis in the population of North China.
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L95 ANSWER 4 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:520753 HCAPLUS
DOCUMENT NUMBER: 143:113964
TITLE: A synthesized cationic tetradecapeptide from hornet venom kills bacteria and neutralizes lipopolysaccharide in vivo and in vitro
AUTHOR(S): Guo, Yibin; Zheng, Jiang; Zhou, Hong; Lu, Gengfa; Wang, Liangxi; **Wei, Guo**; Lu, Yongling
CORPORATE SOURCE: Medical Research Center, Third Military Medical University, Southwest Hospital, Chongqing, 400038, Peop. Rep. China
SOURCE: Biochemical Pharmacology (2005), 70(2), 209-219
CODEN: BCPCA6; ISSN: 0006-2952

PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Sepsis is a complex clin. syndrome that results from a harmful host response to infection, in which foreign bacteria and lipopolysaccharide (LPS) are potent activators of different immune cells, including monocytes and macrophages. To date, there are currently few effective adjuvant therapies in clin. use except activated protein C focusing on the coagulation system. Mastoparans (MPs) are wasp venom cationic amphiphilic tetradecapeptides; these are capable of modulating various cellular activities, including stimulation of GTP-binding protein, phospholipase C and can bind to a phospholipid bilayer. Mastoparan-1 (MP-1, INLKAIAALAKKLL-NH2), a tetradecapeptide toxin isolated from hornet venom, was synthesized chemical In this study, Escherichia coli 25922 (E. coli 25922) and LPS were used to induce sepsis in an animal model. The authors found that MP-1 treatment at 3 mg/kg protected mice from otherwise lethal bacteria and LPS challenges. MP-1 has antibacterial capabilities against Gram-neg. and Gram-pos. bacteria. Its antibacterial action against E. coli may result from the destruction of bacterial membrane structures. In addition, treatment of murine peritoneal macrophages with MP-1 potently inhibited the respiratory burst. This effect maybe related to an inhibition of NADPH oxidase in the membrane. Furthermore, MP-1, bound with high-affinity to LPS and lipid A with dissociation equilibrium consts. of 484
and 456 nM, resp., and neutralized LPS in a dose-dependent manner. MP-1 also significantly reduced the expression of TLR4, TNF-α and IL-6 mRNA and the release of cytokines in LPS-stimulated murine peritoneal macrophages. The results shows that the MP-1-mediated protection of mice from lethal challenge by live bacteria and LPS was associated with its bactericidal action and inhibition of inflammatory responses by macrophages to both bacteria and LPS (the release of cytokines and reactive oxygen species).
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L95 ANSWER 5 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:500303 HCAPLUS
TITLE: Antibacterial activity of mastoparan-1 (MP-1) in vivo and in vitro
AUTHOR(S): Guo, Yibin; Zheng, Jiang; **Wei, Guo**; Lu, Genfa
CORPORATE SOURCE: Southwest Hospital, The Third Military Medical University, Chongqing, 400038, Peop. Rep. China
SOURCE: Zhongguo Kangshengsu Zazhi (2004), 29(8), 454-458, 475
CODEN: ZKZAEY; ISSN: 1001-8689
PUBLISHER: Zhongguo Kangshengsu Zazhishe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The minimal inhibitory concentration (MIC) and minimal bactericidal concentration (MBC)
of MP-1 for 18 tested strains were measured by microdilution method. The morphol. changes of E. coli ATCC25922 were observed after incubated with MP-1 (100 μg/mL) for 5, 10 and 15 min resp. by transmission electron microscope (TEM). The affinity of MP-1 for LPS and Lipid A was assayed by biosensor. In vivo, a LD (2+109CUF/20g body weigh) of viable E. coli ATCC25922 was injected into mice by tail vein, and the activity of MP-1 (3 mg/kg) protecting mice from bacterial challenge were observed Results revealed that the MP-1 antibacterial activity was moderately against Gram-pos. and Gram-neg. bacteria compared with other tested antibiotics. Asymmetry and vacuoles in the cytoplasm of bacteria were

shown after E. coli ATCC25922 was incubated with MP-1 for 5 min, cell swelling for 10 min and severe degeneration for 15 min. MP-1 binded with high-affinity to LPS and Lipid A with dissociation constant (Kd) of 484 nmol and 456 nmol, resp. Moreover, MP-1 could improve the 3-day survival rate of mice from bacterial challenge. MP-1 demonstrated antibacterial activity against Gram-pos. and Gram-neg. bacteria, and its bactericidal action for E. coli ATCC25922 might be caused by the increase in membrane permeability coming from the destruction of membrane structure, which might be based on its affinity for LPS and Lipid A.

L95 ANSWER 6 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:319248 HCAPLUS
DOCUMENT NUMBER: 143:200036
TITLE: The screening and isolation of an effective anti-endotoxin monomer from Radix Paeoniae Rubra using affinity biosensor technology
AUTHOR(S): Lu, Genfa; Zheng, Jiang; Zhou, Hong; Zheng, Yimin; Wang, Liangxi; **Wei, Guo**; Huang, Ming; Jiang, Donglen; Wei, Lizhao
CORPORATE SOURCE: Medical Research Center, Southwestern Hospital, Third Military Medical University, Chongqing, 400038, Peop. Rep. China
SOURCE: International Immunopharmacology (2005), 5(6), 1007-1017
CODEN: IINMBA; ISSN: 1567-5769
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Lipopolysaccharide (LPS) is a known trigger in the pathogenesis of sepsis, lipid A being the toxic component. One of several adjuvant therapeutic approaches for severe sepsis is currently focusing on the neutralization of LPS. In order to obtain the components from traditional Chinese herbs that can neutralize the endotoxin, aqueous extns. were tested using affinity biosensor technol. From amongst 42 herbs, eight were found to possess lipid A-binding abilities. Radix Paeoniae Rubras had the highest lipid A-binding ability; therefore an aqueous extraction from this plant was investigated further. After preparation using standard methods, including silica gel chromatog. and HPLC, we obtained 1, 2, 3, 4, 6-β-D-pentagalloylglucose (PGG), with lipid A-binding ability. It was found that in vitro, PGG directly bound to lipid A, with a Kd of 32 μM, and that it neutralized the endotoxin both in the Limulus Amebocyte Lysate (LAL) assay and in a TNF-α release experiment, in a dose-dependent manner. In in vivo expts., PGG was found to protect mice from a lethal challenge by LPS, and significantly decreased the plasma endotoxin level both in endotoxemic mice and rats, the reduction of the endotoxin level in rats being tightly associated with the TNF-α level. In conclusion, we demonstrate the effectiveness of affinity biosensor technol. in discovering useful agents amongst traditional Chinese herbs and using this approach we found a new anti-endotoxin agent.
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L95 ANSWER 7 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:35625 HCAPLUS
DOCUMENT NUMBER: 142:458735
TITLE: Role of Ets-2 phosphorylation in inflammation, development and cancer

AUTHOR(S): **Wei, Guo**
CORPORATE SOURCE: Ohio State Univ., Columbus, OH, USA
SOURCE: (2004) 276 pp. Avail.: UMI, Order No. DA3115798
From: Diss. Abstr. Int., B 2004, 64(12), 5909
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable

L95 ANSWER 8 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1128120 HCAPLUS
TITLE: Studies on upconversion mechanism of ZrO2:Er3+,Yb3+ nanocrystals under excitation at 488 and 980 nm
AUTHOR(S): Ruo-kun, Jia; Wen-ping, Jian; **Wei, Guo**; Gui-ye, Shan; Qian, Lue; Zhao-yue, Liu; Yu-bai, Bai; Tie-jin, Li; Xiang-gu, Kong
CORPORATE SOURCE: College of Chemistry, Jilin University, Changchun, 130023, Peop. Rep. China
SOURCE: Chemical Research in Chinese Universities (2004), 20(6), 781-784
CODEN: CRCUED; ISSN: 1005-9040
PUBLISHER: Higher Education Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB ZrO2:Er3+,Yb3+ nanoparticles were prepared by the sol-emulsion gel technique. The purpose of the present study is the application of upconversion phosphor in the biol. label. To make out the mechanism of upconversion under 980 nm excitation the 488 nm pump was used. The influence of temperature on the crystallite phase was studied. The upconverted mechanism in ZrO2:Er3+,Yb3+ nanocrystals is due to an energy transfer upconversion.
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L95 ANSWER 9 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1086778 HCAPLUS
DOCUMENT NUMBER: 142:91895
TITLE: The Serine/Threonine Kinase Akt Promotes Fcγ Receptor-mediated Phagocytosis in Murine Macrophages through the Activation of p70 S6 Kinase
AUTHOR(S): Ganesan, Latha P.; **Wei, Guo**; Pengal, Ruma A.; Moldovan, Leni; Moldovan, Nicanor; Ostrowski, Michael C.; Tridandapani, Susheela
CORPORATE SOURCE: Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Department of Molecular Genetics, Molecular, Cellular, and Developmental Biology Program, Ohio State University, Columbus, OH, 43210, USA
SOURCE: Journal of Biological Chemistry (2004), 279(52), 54416-54425
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Fcγ receptor (FcγR) clustering by immune complexes activates multiple signaling pathways leading to phagocytosis. The authors and others have previously reported that Akt is phosphorylated in response to FcγR clustering. However, the functional consequence of Akt activation by FcγR is not known. Using Raw 264.7 macrophage cells transfected to overexpress either constitutively active myristoylated

(Myr)-Akt or a dominant-neg. CAAX-Akt and bone marrow macrophages (BMMs) from wild-type and transgenic mice expressing macrophage-specific Myr-Akt, the authors analyzed the function of Akt in phagocytosis. The authors report that overexpression of Myr-Akt resulted in significant increase in phagocytic efficiency, whereas CAAX-Akt down-regulated phagocytosis in Raw 264.7 cells. Likewise BMMs expressing Myr-Akt displayed enhanced phagocytic ability. Analyzing the downstream effectors of Akt, the authors demonstrate that p70S6 kinase is constitutively phosphorylated in Myr-Akt-expressing BMMs. P70S6 kinase is reported to influence actin cytoskeleton and cell migration, suggesting that Akt may influence phagocytosis through the activation of p70S6 kinase. Consistent with this, overexpression of either wild-type or constitutively active but not a kinase-inactive p70S6 kinase in Raw 264.7 cells significantly enhanced phagocytosis. Likewise suppression of p70S6 kinase with rapamycin down-regulated phagocytic efficiency conferred by the expression of constitutively active Akt. These findings demonstrate a novel role for Akt in phagocytosis through the activation of p70S6 kinase.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L95 ANSWER 10 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1086127 HCAPLUS
DOCUMENT NUMBER: 142:290982
TITLE: Study of anti-endotoxin effect of polymyxin B in vitro
AUTHOR(S): Lu, Genfa; **Wei, Guo**; Guo, Yibin; Xiao, Guangxia; Zheng, Jiang; Luo, Gaoxing
CORPORATE SOURCE: Southwest Hospital, Third Military Medical University, Chongqing, 400038, Peop. Rep. China
SOURCE: Di-San Junyi Daxue Xuebao (2004), 26(14), 1252-1254
CODEN: DYXUE8; ISSN: 1000-5404
PUBLISHER: Di-San Junyi Daxue Xuebao Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB To investigate the effects of polymyxin B (PMB) on the affinity and neutralization with lipid A and the anti- lipopolysaccharide (LPS) effect of PMB, the ability of PMB on endotoxin-neutralization was detected by quant. limulus amoebocyte lysate assay. The affinity for lipid A was detected by biosensor technol. The inhibitory effects of PMB on tumor necrosis factor alpha (TNF-α) and interleukin 6 (IL-6) released from LPS-stimulated human peripheral blood mononuclear cell (PBMC) were detected by ELISA. The results showed that PMB had high anti-LPS ability, and the inhibition concentration at 50% endotoxin was (4.35±0.91) μmol/L. PMB also had high affinity for lipid A, and the KD value for lipid A was 1.11+10-8 mol/L. PMB at the dose of 10 μg/mL had significantly inhibitory effect on TNF-α and IL-6 release induced by 100 ng/mL LPS ($P<0.05$) in a dose-effect manner. At 10 min after LPS stimulation, PMB could hardly inhibit the release of TNF-α and IL-6. PMB has high binding and neutralizing abilities of LPS and can inhibit the release of TNF-α and IL-6 in time- and dose-dependent manners.

L95 ANSWER 11 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:863539 HCAPLUS
DOCUMENT NUMBER: 142:1995
TITLE: The mitochondrial toxin, 3-nitropropionic acid, induces extracellular Zn2+ accumulation in rat hippocampus slices
AUTHOR(S): **Wei, Guo**; Hough, Christopher J.; Sarvey, John M.
CORPORATE SOURCE: Department of Pharmacology, Uniformed Services University of Health Sciences, Bethesda, MD, 20814,

USA
SOURCE: Neuroscience Letters (2004), 370(2-3), 118-122
CODEN: NELED5; ISSN: 0304-3940
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 3-Nitropropionic acid (3-NPA), a suicide inhibitor of succinate dehydrogenase (SDH; complex II), has been used to provide useful exptl. models of Huntington's disease (HD) and "chemical hypoxia" in rodents. The trace ion Zn2+ has been shown to cause neurodegeneration. Employing real-time Newport Green fluorescence imaging of extracellular Zn2+, we found that 3-NPA (10-100 μM) caused a concentration-dependent increase in the concentration of extracellular Zn2+ ([Zn2+]o) in acute rat hippocampus slices. This increase in [Zn2+]o was abolished by 10 mM CaEDTA. The increase of [Zn2+]o was also accompanied by a rapid increase of cytoplasmic-free Zn2+ concentration ([Zn2+]i). The induction of Zn2+ release by 3-MPA in hippocampus slices points to a potential mechanism by which 3-NPA might induce neurodegeneration.
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L95 ANSWER 12 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:826738 HCAPLUS
DOCUMENT NUMBER: 142:276313
TITLE: Study of biosensor technology on detection of endotoxin-neutralizing materials
AUTHOR(S): Lu, Genfa; Gong, Xiaoyun; **Wei, Guo**; Wang, Ning; Xiao, Guangxia; Zheng, Jiang
CORPORATE SOURCE: Southwest Hospital, Third Military Medical University, Chongqing, 400038, Peop. Rep. China
SOURCE: Zhonghua Shaoshang Zazhi (2004), 20(1), 23-25
CODEN: ZSZHA5; ISSN: 1009-2587
PUBLISHER: Zhonghua Shaoshang Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB After mixing polymyxin B (PMB) with endotoxin (lipopolysaccharides, LPS) in certain concentration, the neutralizing ratio of PMB to endotoxin was assessed by biosensor technique and limulus amebocyte lysate test, resp. The results from the two methods were compared. The neutralizing ratio of PMB to endotoxin as assessed by biosensor technol. was 0.35 μg to 1 ng, while that by dynamic turbidimetric and chromogenic limulus amebocyte lysate (LAL) technique was 0.5 mg to 1 ng and 1 mg to 1 ng, resp. The results obtained by biotechnol. were similar to that by biosensor technique. Biosensor technol. was an accurate, convenient and rapid method for the determination of potency of endotoxin-neutralizing materials.

L95 ANSWER 13 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:545196 HCAPLUS
DOCUMENT NUMBER: 141:139103
TITLE: Activated Ets2 Is Required for Persistent Inflammatory Responses in the Motheaten Viable Model
AUTHOR(S): **Wei, Guo**; Guo, Jianping; Doseff, Andrea I.; Kusewitt, Donna F.; Man, Albert K.; Oshima, Robert G.; Ostrowski, Michael C.
CORPORATE SOURCE: Department of Molecular Genetics, Ohio State University, Columbus, OH, 43210, USA
SOURCE: Journal of Immunology (2004), 173(2), 1374-1379
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists

DOCUMENT TYPE: Journal
LANGUAGE: English
AB The Ets2 transcription factor is constitutively phosphorylated on residue Thr72 in macrophages derived from mice homozygous for the motheaten viable (me-v) allele of the hemopoietic cell phosphatase (Hcph) gene. To genetically test the importance of signaling through residue Thr72 of Ets2 during inflammation, the Ets2A72 mutant allele, which cannot be phosphorylated on Thr72, was combined with the Hcphme-v allele in mice. Ets2A72/A72 moderated the inflammation-related pathol. of Hcphme-v/me-v mice, as demonstrated by the increased life span and the decreased macrophage infiltration in skin and lungs of these mice. Macrophage apoptosis induced by cytokine withdrawal was also increased in the double-mutant mice. Importantly, the Ets2A72/A72 allele resulted in decreased expression of inflammatory response genes, including TNF-α, CCL3, matrix metalloprotease 9, integrin αM, and Bcl-X in alveolar macrophage. Ets2 phosphorylation was required for persistent activation of TNF-α following LPS stimulation of bone marrow-derived macrophages. The phosphorylation of Ets2 functions in the severe inflammatory phenotype of the me-v model by mediating both macrophage survival and inflammatory gene expression.
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L95 ANSWER 14 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:513539 HCAPLUS
DOCUMENT NUMBER: 141:71457
TITLE: A preparation of 2-aminocarbonylquinoline derivatives, useful as platelet adenosine diphosphate receptor antagonists
INVENTOR(S): Bryant, Judi; Buckman, Brad; Islam, Imadul; Mohan, Raju; Morrissey, Michael; **Wei, Guo Ping**; Xu, Wei; Yuan, Shendong
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004052366	A1	20040624	WO 2003-US39079		20031209
WO 2004052366	C2	20050623			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2507657	AA	20040624	CA 2003-2507657		20031209
US 2004138229	A1	20040715	US 2003-731815		20031209
PRIORITY APPLN. INFO.:			US 2002-432792P	P	20021211
			WO 2003-US39079	W	20031209

OTHER SOURCE(S): MARPAT 141:71457
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to 2-aminocarbonylquinoline derivs. of formula I [wherein: R1 is H, alkyl, carboxyalkyl, aryl, arylalkyl, or heterocyclylcarbonyl, etc.; R2 is H, alkyl, aryl, alkylsulfonylalkyl, aminoalkyl, or carboxyalkylthioalkyl, etc.; R3 is (un)substituted aryl or aryloxy; R4 is H, alkyl, alkoxy, halo, haloalkyl, OH, CN, or alkylthio, etc.; R5 is H, alkyl, hydroxyalkyl, carboxy, or arylalkyl, etc.; R6 is H, alkyl, or carboxyalkyl, etc.], useful as inhibitors of platelet ADP. Receptor binding and ADP-induced aggregation studies were performed (no biol. data). Inhibition of thrombus formation by the invention compds. was evaluated in the rat arterio-venous shunt model (no biol. data). For instance, quinoline derivative II (X = n-Pr) was prepared via amidation of 2-carboxy-4-benzyloxyquinoline by the prepared amine III and subsequent benzyloxycarbonyl cleavage of the obtained II [X = (CH2)3C(O)OBn].

L95 ANSWER 15 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:280214 HCAPLUS
DOCUMENT NUMBER: 140:373838
TITLE: The Inositol 3-Phosphatase PTEN Negatively Regulates Fcγ Receptor Signaling, but Supports Toll-Like Receptor 4 Signaling in Murine Peritoneal Macrophages
AUTHOR(S): Cao, Xianhua; **Wei, Guo**; Fang, Huiqing; Guo, Jianping; Weinstein, Michael; Marsh, Clay B.; Ostrowski, Michael C.; Tridandapani, Susheela
CORPORATE SOURCE: Biophysics Program, Ohio State University, Columbus, OH, 43210, USA
SOURCE: Journal of Immunology (2004), 172(8), 4851-4857
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English
AB FcγR clustering in macrophages activates signaling events that result in phagocytosis. Phagocytosis is accompanied by the generation harmful byproducts such as reactive oxygen radicals and production of inflammatory cytokines, which mandate that the phagocytic process be subject to a tight regulation. The mol. mechanisms involved in this regulation are not fully understood. In this study, the authors have examined the role of the inositol 3-phosphatase and tensin homolog deleted on chromosome 10 (PTEN) in FcγR-induced macrophage function. The authors demonstrate that in ex vivo murine peritoneal macrophages that are deficient in PTEN expression, FcγR-induced Akt and extracellular signal-regulated kinase phosphorylation are enhanced. Notably, PTEN-/- macrophages showed constitutively high phosphorylation of Akt. However, PTEN did not seem to influence tyrosine phosphorylation events induced by FcγR clustering. Furthermore, PTEN-/- macrophages displayed enhanced phagocytic ability. Likewise, FcγR-induced production of TNF-α, IL-6, and IL-10 was significantly elevated in PTEN-/- macrophages. Surprisingly, LPS-induced TNF-α production was down-regulated in PTEN-/- macrophages. Analyzing the mol. events leading to PTEN influence on LPS/Toll-like receptor 4 (TLR4) signaling, the authors found that LPS-induced activation of mitogen-activated protein kinases is suppressed in PTEN-/- cells. Previous reports indicated that LPS-induced mitogen-activated protein kinase activation is down-regulated by phosphatidylinositol 3-kinase through the activation of Akt. The authors' observation that Akt activation is basally enhanced in PTEN-/-

cells suggests that PTEN supports TLR4-induced inflammatory responses by suppressing the activation of Akt. Thus, the authors conclude that PTEN is a neg. regulator of FcγR signaling, but a pos. regulator of TLR4 signaling. These findings are the first to demonstrate a role for PTEN in FcγR- and TLR4-mediated macrophage inflammatory response.
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L95 ANSWER 16 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:235455 HCAPLUS
DOCUMENT NUMBER: 140:392960
TITLE: Study on the analytical method of igniting composition BNP
AUTHOR(S): Rao, Yu'e; Zhang, Aihua; **Wei, Guo**
CORPORATE SOURCE: The 213th Research Institute of China Ordnance Industry, Xian, 710061, Peop. Rep. China
SOURCE: Huogongpin (2003), (2), 50-52
CODEN: HUOGE5; ISSN: 1003-1480
PUBLISHER: Huogongpin Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The anal. method of determining the contents of main components of KNO3 and powdered boron in BNP was introduced. In view of the ultrafine nature of powdered B, the method combined the gravimetric method and volumetric method together. Test results showed that accuracy and precision are high. It is simple and feasible method.

L95 ANSWER 17 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:196485 HCAPLUS
DOCUMENT NUMBER: 140:385675
TITLE: Novel 3-Oxa Lipoxin A4 Analogues with Enhanced Chemical and Metabolic Stability Have Anti-inflammatory Activity in Vivo
AUTHOR(S): Guilford, William J.; Bauman, John G.; Skuballa, Werner; Bauer, Shawn; **Wei, Guo Ping**; Davey, David; Schaefer, Caralee; Mallari, Cornell; Terkelsen, Jennifer; Tseng, Jih-Lie; Shen, Jun; Subramanyam, Babu; Schottelius, Arndt J.; Parkinson, John F.
CORPORATE SOURCE: Departments of Medicinal Chemistry, Immunology, Animal Pharmacology and Pharmacokinetics and Drug Metabolism, Berlex Biosciences, Richmond, CA, 94804, USA
SOURCE: Journal of Medicinal Chemistry (2004), 47(8), 2157-2165
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Lipoxin A4 (LXA4) is a structurally and functionally distinct natural product called an eicosanoid, which displays immunomodulatory and anti-inflammatory activity but is rapidly metabolized to inactive catabolites in vivo. A previously described analog of LXA4, Me 16-(4-fluorophenoxy)-5,6,15-trihydroxy-7,9,11,13-hexadecatetraenoate (2, ATLa), was shown to have a poor pharmacokinetic profile after both oral and i.v. administration, as well as sensitivity to acid and light. The chemical stability of the corresponding E,E,E-trien-11-yne analog, 3, was improved over 2 without loss of efficacy in the mouse air pouch model of inflammation. Careful anal. of the plasma samples from the pharmacokinetic assays for both 2 and 3 identified a previously undetected metabolite, which is consistent with metabolism by β-oxidation The formation of the oxidative metabolites was eliminated with the

corresponding 3-oxatetraene, 4, and the 3-oxatrien-11-yne, 5, analogs of 2. Evaluation of 3-oxa analogs 4 and 5 in calcium ionophore-induced acute skin inflammation model demonstrated similar topical potency and efficacy compared to 2. The 3-oxatrien-11-yne analog, 5, is equipotent to 2 in an animal model of inflammation but has enhanced metabolic and chemical stability and a greatly improved pharmacokinetic profile.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L95 ANSWER 18 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:985665 HCAPLUS
DOCUMENT NUMBER: 140:258112
TITLE: Elimination of nocuous elements from waste Zn-Mn dry battery
AUTHOR(S): **Wei, Guo**; Zhang, Li-hua; Zhao, Deng-bao; Shen, Feng-man
CORPORATE SOURCE: School of Materials & Metallurgy, Northeastern University, Shenyang, 110004, Peop. Rep. China
SOURCE: Dongbei Daxue Xuebao, Ziran Kexueban (2003), 24(7), 689-691
CODEN: DDXKEZ; ISSN: 1005-3026
PUBLISHER: Dongbei Daxue Xuebao Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB The pyrogenic process and wet process were used to remove Cl and Zn which have neg. effect on blast furnace operation in battery recycle. Results show that in the range of experiment, pyrogenic process can remove most of Cl but has no effect on Zn. Higher removal efficiency can be obtained at higher temps. and Cl was removed by 37% at 615 K. The removal effect of wet process is better than the pyrogenic process. Under the condition of 15 min, wet process can remove Cl by 85% and Zn by 30% at 318 K. In the wet process, temperature and time have little effect on the results so it is convenient for industrial application. Dry batteries treated by the wet process can meet the stds. of blast furnace operation so that they can be used as additives for pulverized coal injection.

L95 ANSWER 19 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:952279 HCAPLUS
DOCUMENT NUMBER: 141:22005
TITLE: Effect of recombinant chemokine vMPII on survival of allo-skin in mice
AUTHOR(S): Zheng, Hong; Su, Qinghe; Sun, Zhicheng; Feng, Wenxi; Cao, Chuan; Cao, Hongwei; Zhao, Jingyi; Zhong, Baiyu; Deng, Yongjian; Luo, Ping; **Wei, Guo**; Wu, Jun
CORPORATE SOURCE: Southwest Hospital, Third Military Medical University, Chongqing, 400038, Peop. Rep. China
SOURCE: Di-San Junyi Daxue Xuebao (2002), 24(9), 1013-1016
CODEN: DYXUE8; ISSN: 1000-5404
PUBLISHER: Di-San Junyi Daxue Xuebao Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB Whether the recombinant chemokine vMIPII possesses the capability of inhibiting allo-skin transplantation rejection and prolonging the survival of the allograft in mic were investigated. A thioredoxin-vMIPII fusion protein(26+103) was expressed in E. coli under induction of IPTG when pET32a-vMIPII was used as an expression vector. The purified vMIPII was produced through metal-chelated affinity chromatog., enterokinase digestion to free vMIPII from fusion protein and cation exchange chromatog. Its ability of binding with its receptor CCR5 was testified by using ligand-binding assay. The purified vMIPII was injected in tail vein

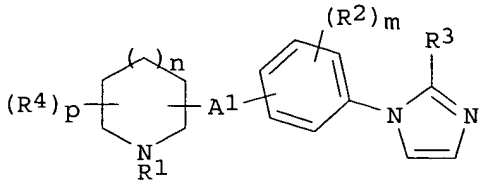
once everyday after skin transplantation (Kunming mice to Balb/c) till the 14th day. High purified vMIPII was obtained from fermented bacteria. It bound with CCR5 expressed on CHO cells with a dissociate constant (Kd) of (11.56) nmol/L. The allo-skins of the mice which were injected with vMIPII survived 7 d longer than those with salt saline injection. Purified recombinant vMIPII is capable of inhibiting the allo-graft rejection in mouse allo-skin transplantation, and markedly prolonging the survival of the allo-skin.

L95 ANSWER 20 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:892605 HCAPLUS
DOCUMENT NUMBER: 139:381481
TITLE: Preparation of arylimidazoles as nitric oxide synthase (NOS) inhibitors
INVENTOR(S): Davey, David D.; Mohan, Raju; Phillips, Gary B.; **Wei, Guo Ping**; Xu, Wei
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

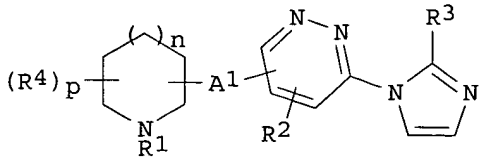
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003092678	A1	20031113	WO 2003-US12740	20030424
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004023950	A1	20040205	US 2003-422185	20030423
EP 1501504	A1	20050202	EP 2003-726440	20030424
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.: US 2002-377274P P 20020430
WO 2003-US12740 W 20030424

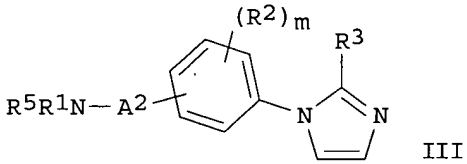
OTHER SOURCE(S): MARPAT 139:381481
GI



I



II



III

AB Title compds. [I, II, III; n = 0-2; m = 0-4; p = 0-2; q = 0-3; r = 2, 3; t = 0-6; A1 = O(CH2)q, NR6(CH2)q; A2 = (CH2)rO; R1 = H, alkyl, (CH2)tCO2R7, (CH2)tCONR6R7, COR7, (substituted) aralkyl, heterocyclylalkyl; R2 = halo, haloalkyl, alkyl, NO2, OR6, CO2R6, NR6R7, etc.; R3 = H, alkyl; R4 = alkyl, halo, haloalkyl, OH, aralkoxy, aryl, NO2, amino, etc.; R5 = H, alkyl, aralkyl, (substituted) heterocyclylalkyl, etc.; R6, R7 = H, alkyl, (substituted) aryl, aralkyl, heterocyclyl, etc.], were prepared as drugs (no data). Thus, a mixture of (3S)-3-(4-aminophenoxy)-1-[(1,3-benzodioxol-5-yl)methyl]piperidine and NH4OH in MeOH and a solution of formaldehyde and 40% glyoxal in THF were added simultaneously to H2O at 65° with stirring over a 30 min. period. The resulting mixture was then heated to 65° for 2 h to give 72.5% (3S)-3-[4-(imidazol-1-yl)phenoxy]-1-[(1,3-benzodioxol-5-yl)methyl]piperidine.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L95 ANSWER 21 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:703610 HCAPLUS

DOCUMENT NUMBER: 140:263798

TITLE: Affinities of peptide (BNEP) mimicking bactericidality/permeability-increasing protein for lipopolysaccharide and lipid A by biosensor technology

AUTHOR(S): Zheng, Jiang; Gong, Xiaoyun; Lu, Genfa; **Wei, Guo**; Zhou, Hong

CORPORATE SOURCE: Medical Research Center, Southwest Hospital, Third Military Medical University, Chungking, 400038, Peop. Rep. China

SOURCE: Jiefangjun Yixue Zazhi (2003), 28(3), 197-199
CODEN: CFCHBN; ISSN: 0577-7402

PUBLISHER: Jenminjun Chubanshe

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

AB The mechanism of bactericidal neutralizing endotoxin peptide (BNEP), a synthetic peptide mimicking bactericidality/permeability-increasing protein (BPI), was studied. The affinities of BNEP for LPS and Lipid A

were determined with biosensor technol., and the ability of BNEP neutralizing LPS in vitro was tested by quant. limulus amoebocyte lysate assay. The results showed that BNEP had high affinities for both LPS and Lipid A. The Kd value for LPS was at the level between 25.8 and 48.8 nmol/L and for Lipid A from 11.8 to 21.8 nmol/L. When 8 μg/mL of BNEP was used, it could completely neutralize the concentration of 2 ng/mL of LPS in vitro. It is concluded that BNEP has high binding affinities for both LPS and Lipid A. The binding site of LPS is at the glucosaminyl-β1'-6- glucosamine disaccharide of Lipid A. The binding activity of BNEP for LPS is in accord with its neutralizing activity for LPS.

L95 ANSWER 22 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:695801 HCAPLUS
DOCUMENT NUMBER: 139:322489
TITLE: A multifunctional sensor for concentrations of ternary solution with NaCl and sucrose employed in osmotic dehydration process
AUTHOR(S): **Wei, Guo**; Shida, Katsunori
CORPORATE SOURCE: Department of Electrical and Electronic Engineering, Faculty of Science and Engineering, Saga University, Saga, 840-8502, Japan
SOURCE: Japanese Journal of Applied Physics, Part 1: Regular Papers, Short Notes & Review Papers (2003), 42(8), 5361-5366
CODEN: JAPNDE
PUBLISHER: Japan Society of Applied Physics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors present a multifunctional sensor capable of directly sensing temperature and two phys. parameters of solns., namely ultrasonic velocity and elec. conductivity By combination measurement of these three measurable parameters, the concns. of various components in ternary solution with NaCl and sucrose can be simultaneously determined A regression algorithm based on natural cubic spline interpolation and the least squares method is developed to estimate the concns. of NaCl and sucrose, which considers the temperature influence on the multifunctional sensor and then enables decoupling of the reconstruction of concns. in 4D space into 3D space. This sensor could prove valuable as a process control sensor in food industry.
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L95 ANSWER 23 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:658837 HCAPLUS
DOCUMENT NUMBER: 139:302861
TITLE: Ets-2 interacts with co-repressor BS69 to repress target gene expression
AUTHOR(S): **Wei, Guo**; Schaffner, Alicia Erbe; Baker, Kimberly M.; Mansky, Kim C.; Ostrowski, Michael C.
CORPORATE SOURCE: Department of Molecular Genetics and The Comprehensive Cancer Center, Ohio State University, Columbus, OH, 43210, USA
SOURCE: Anticancer Research (2003), 23(3A), 2173-2178
CODEN: ANTRD4; ISSN: 0250-7005
PUBLISHER: International Institute of Anticancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The ETS family of proteins consists of over 30 members that regulate the growth, differentiation and survival of both normal and tumor cells. How specificity is achieved within this family remains largely unresolved.

One mechanism for attaining specificity is through the action of signaling pathways on specific family members. For example, Ets-2 is an activator modulated by ras-dependent phosphorylation of a single residue in the conserved pointed domain of this factor. We hypothesized that phosphorylation of the pointed domain regulates the proteins that can interact with ets-2 in the cell nucleus, resulting in regulation of target genes. We used a combination of biochem. assays, yeast two-hybrid screens and transfection assays to identify and characterize proteins interacting with the pointed domain. BS69, a known co-repressor, was identified in a yeast two hybrid screen as an ets-2 interacting partner. BS69 can interact with ets-2 in vivo and phosphorylation of the ets-2 pointed domain decreased the interaction with BS69 in vitro. In transfection assays, co-expression of ets-2 and BS69 resulted in repression of defined ets-2 target genes. These results support a role for ets-2 as a repressor and indicate that BS69 is required as co-repressor. Phosphorylation of ets-2 may switch its activity from repressor to activator by interfering with formation of the BS69 complex.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L95 ANSWER 24 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:611990 HCAPLUS
DOCUMENT NUMBER: 139:399043
TITLE: Zr loaded waste ion-exchange resin for fluoride removal
AUTHOR(S): Zhang, Yu; **Wei, Guo**; Yang, Min; Gao, Yingxin
CORPORATE SOURCE: Research Center for Eco-Environmental Sciences, Chinese Academy of Sciences, Beijing, 100085, Peop. Rep. China
SOURCE: Huanjing Wuran Zhili Jishu Yu Shebei (2002), 3(5), 45-48
CODEN: HWZJAB; ISSN: 1008-9241
PUBLISHER: Huanjing Wuran Zhili Jishu Yu Shebei Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB A ZrO2 based adsorbent loaded on waste ion-exchange resin from a thermal power plant was developed, and its performance for fluoride removal was evaluated with beaker and column tests. A concentration of ZrOCl2 at 0.5 mol/L was proper for loading Zr on the resins. The optimum pH for adsorption in beaker test was 3.0-4.0. In the column test, however, the adsorption performance at pH 3.0 was significantly better than that at pH 4.0. Two columns connected in series were used for the removal of fluoride from thermal power plant wastewater under a SV of 10 (single bed). The 1st column reached the breakthrough point in 410 bed vols., and the 2nd column reached the point in 1500 bed vols. The breakthrough capacities, however, decreased to some extent after regeneration with 0.1 mol/L NaOH solution

L95 ANSWER 25 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:498065 HCAPLUS
DOCUMENT NUMBER: 139:259160
TITLE: Hearts From Rodents Exposed to Intermittent Hypoxia or Erythropoietin Are Protected Against Ischemia-Reperfusion Injury
AUTHOR(S): Cai, Zheqing; Manalo, Dominador J.; **Wei, Guo**; Rodriguez, E. Rene; Fox-Talbot, Karen; Lu, Huasheng; Zweier, Jay L.; Semenza, Gregg L.
CORPORATE SOURCE: McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, USA
SOURCE: Circulation (2003), 108(1), 79-85

CODEN: CIRCAZ; ISSN: 0009-7322
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background- Preconditioning phenomena provide evidence for adaptive responses to ischemia that have important implications for treatment/prevention of myocardial infarction. Hypoxia-inducible factor 1 (HIF-1) mediates adaptive transcriptional responses to hypoxia/ischemia. Methods and Results- Exposure of wild-type mice to intermittent hypoxia resulted in protection of isolated hearts against ischemia-reperfusion injury 24 h later. Cardiac protection induced by intermittent hypoxia was lost in Hif1a+/- mice heterozygous for a knockout allele at the locus encoding HIF-1α. Erythropoietin (EPO) mRNA expression was induced in kidneys of wild-type mice subjected to intermittent hypoxia, resulting in increased plasma EPO levels. EPO mRNA expression was not induced in Hif1a+/- mice. EPO administration to rats increased functional recovery and decreased apoptosis in isolated hearts subjected to ischemia-reperfusion 24 h later. Conclusions- Hearts isolated from rodents subjected to intermittent hypoxia or EPO administration are protected against postischemic injury. Cardiac protection induced by intermittent hypoxia is critically dependent on Hif1a gene dosage. The authors' data suggest that addnl. studies to evaluate therapeutic applications of EPO administration are warranted.
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L95 ANSWER 26 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:366165 HCAPLUS
DOCUMENT NUMBER: 139:64245
TITLE: Ets-2 and Components of Mammalian SWI/SNF Form a Repressor Complex That Negatively Regulates the BRCA1 Promoter
AUTHOR(S): Baker, Kimberly M.; **Wei, Guo**; Schaffner, Alicia Erbe; Ostrowski, Michael C.
CORPORATE SOURCE: Department of Molecular Genetics and The Comprehensive Cancer Center, Ohio State University, Columbus, OH, 43210, USA
SOURCE: Journal of Biological Chemistry (2003), 278(20), 17876-17884
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ets-2 is a transcriptional activator that can be modulated by ras-dependent phosphorylation. Evidence is presented indicating that ets-2 can also act as a transcriptional repressor. In the breast cancer cell line MCF-7, exogenous ets-2 repressed the activity of a BRCA1 promoter-luciferase reporter dependent on a conserved ets-2-binding site in this promoter. Conditional overprodn. of ets-2 in MCF-7 cells resulted in repression of endogenous BRCA1 mRNA expression. To address the mechanism by which ets-2 could act as a repressor, a biochem. approach was used to identify proteins that interacted with the ets-2 pointed domain. From this anal., components of the mammalian SWI/SNF chromatin remodeling complex were found to interact with ets-2. Brg-1, the ATP-hydrolyzing component of the SWI/SNF complex, along with the BAF57/p50 and Ini1 subunits could be co-immunopptd. from cells with ets-2. The pointed domain of ets-2 directly interacted in vitro with the C-terminal region of Brg-1 in a phosphorylation-dependent manner. The combination of Brg-1 and ets-2 could repress the BRCA1 promoter reporter in transfection assays.

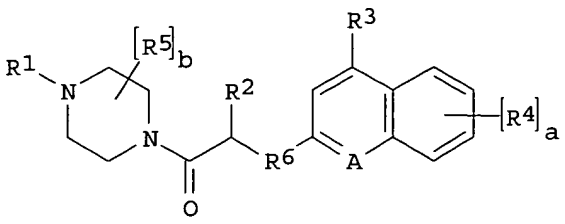
These results support a role for ets-2 as a repressor and indicate that components of the mammalian SNF/SWI complex are required as co-repressors.
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L95 ANSWER 27 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:946267 HCAPLUS
DOCUMENT NUMBER: 138:24727
TITLE: Preparation of 2-[(piperazinocarbonylmethyl)aminocarbonyl]quinolines as platelet adenosine diphosphate receptor antagonists
INVENTOR(S): Bryant, Judi A.; Buckman, Brad O.; Islam, Imadul; Mohan, Raju; Morrissey, Michael M.; **Wei, Guo Pin**; Xu, Wei; Yuang, Shendong
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 208 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002098856	A2	20021212	WO 2002-US17821	20020606
WO 2002098856	A3	20040304		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003060474	A1	20030327	US 2002-163742	20020605
US 6861424	B2	20050301		
EP 1412349	A2	20040428	EP 2002-746471	20020606
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004532886	T2	20041028	JP 2003-501845	20020606
US 2005038037	A1	20050217	US 2004-947579	20040922
US 2005065163	A1	20050324	US 2004-947635	20040922

PRIORITY APPLN. INFO.:	US 2001-296498P	P	20010606
	US 2002-163742	A	20020605
	WO 2002-US17821	W	20020606

OTHER SOURCE(S): MARPAT 138:24727
GI



I

AB The title compds. [I; a, b = 1-4; A = CH, N; R1 = H, alkyl, aryl, etc.; R2 = H, alkyl, aryl, etc.; R3 = H, alkyl, OH, etc.; R4 = H, alkyl, alkoxy, etc.; R5 = H, alkyl, hydroxyalkyl, etc.; R6 = NR7CO, CONR7; R7 = H, alkyl, carboxyalkyl, alkoxycarbonylalkyl], useful as inhibitors of platelet aggregation and thrombus formation, were prepared and formulated. Thus, amidation of 7-methyl-4-hydroxy-2-carboxyquinoline with 4-ethoxycarbonyl-1-[1-amino-3-(1,1-dimethylethoxycarbonyl)propyl]carbonylpiperazine (preparation of both reactants given) afforded 68% I [R1 = CO2Et; R2 = tert-BuOCOCH2CH2; R3 = OH; R4 = 7-Me; R5 = H; R6 = NHCO; A = N]. The compds. I demonstrated their ability to inhibit the binding of [33P]-2-methylthio-ADP binding to the human platelet ADP receptor and the rat platelet ADP receptor.

L95 ANSWER 28 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:677794 HCAPLUS
DOCUMENT NUMBER: 138:92498
TITLE: Relationship between fractal dimension and burnout of pulverized coal
AUTHOR(S): **Wei, Guo**; Yang, Jun-he; Du, He-gui; Liu, Zhen-yi
CORPORATE SOURCE: School of Materials & Metallurgy, Northeastern University, Shenyang, 110004, Peop. Rep. China
SOURCE: Dongbei Daxue Xuebao, Ziran Kexueban (2002), 23(3), 240-242
CODEN: DDXKEZ; ISSN: 1005-3026
PUBLISHER: Dongbei Daxue Xuebao Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB A combustion experiment was carried out to study the relationship between the structure of pulverized coal and its burnout in blast furnace. To describe the structure of coal particle, Ds (fractal dimension), was defined based on fractal theory. The Ds varies with coal. The Ds value for bituminite is higher than that for anthracite on the whole. The burnout performance of coal is mainly affected by its volatile matter yield. The Ds is related to the combustion ratio of pulverized coal. For coals of similar approx. anal. data, a higher combustion rate is obtained for the one with higher Ds value. The maceral form and content have great impact on the structure fractal dimension.

L95 ANSWER 29 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:669140 HCAPLUS
DOCUMENT NUMBER: 136:367496
TITLE: Detection of HBV DNA with fluorescence quantitative PCR and its clinical significance
AUTHOR(S): Cao, Hongwei; **Wei, Guo**; Feng, Wenyi; Gong, Xiaoyun; Zheng, Jiang
CORPORATE SOURCE: Centre Laboratory, Xinan Hospital, Third Military Medical University, Chungking, 400038, Peop. Rep. China
SOURCE: Di-San Junyi Daxue Xuebao (2001), 23(7), 866-868
CODEN: DYXUE8; ISSN: 1000-5404
PUBLISHER: Di-San Junyi Daxue
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The correlation between hepatitis B virus (HBV) DNA and HBV biomarkers was studied. HBV biomarkers and HBV DNA were simultaneously detected by PCR in 362 sera of hepatitis B patients. The pos. rate and copy number of HBV DNA were 97.7% and 104-108 in HBsAg, HBeAg, and HBcAb pos. groups, 56% and

102-107 in HBsAg, HBeAb, and HBcAb pos. group, 54% and 102-107 in HBsAg and HBcAb pos. group, and 100% and 107 in HBsAg and HBeAg pos. group, resp. The pos. rate and copy number of HBV DNA were 1/3 and 102 in HBeAb and HBcAb pos. group, 14.3% and 103-107 in HBsAb pos. group, and 2/189 (1.06%) and 104-105 in normal control, resp. The results showed that HBV DNA may be detectable in sera of various HBV biomarkers but detection ratio was significantly different (1.06-100%), pos. rate and copy number of HBV DNA in HBeAg pos. group were the highest, HBV DNA was detectable in HBsAg and its antibody pos. groups, and it was insufficient to use HBV biomarkers for early diagnosis of HBV infection.

L95 ANSWER 30 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:309179 HCAPLUS
DOCUMENT NUMBER: 134:331713
TITLE: Analysis of ginsenosides in Panax quinquefolium by HPLC-ELSD
AUTHOR(S): Jiang, Yingqiao; Wang, Qiang; **Wei, Guo**; Huang, Quanming
CORPORATE SOURCE: Department of Chinese Materia Medica Analysis, China Pharmaceutical University, Nanjing, 210038, Peop. Rep. China
SOURCE: Zhongguo Yaoke Daxue Xuebao (2001), 32(1), 41-43
CODEN: ZHYXE9; ISSN: 1000-5048
PUBLISHER: Zhongguo Yaoke Daxue
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The content of ginsenosides in Panax quinquefolium was determined by HPLC-ELSD detector on a LiChrosorb NH2 column with MeCN-H2O-iso-PrOH and water as gradient eluents. The average recovery was 95.97-100.05% and relative standard deviation 0.87-2.75%. The method was simple, accurate, and reliable for the quality control of P. quingquefolium.

L95 ANSWER 31 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:227606 HCAPLUS
DOCUMENT NUMBER: 135:3635
TITLE: Nitric oxide and peroxynitrite in postischemic myocardium
AUTHOR(S): Zweier, Jay L.; Fertmann, Jan; **Wei, Guo**
CORPORATE SOURCE: Molecular and Cellular Biophysics Laboratories, Department of Medicine, Division of Cardiology and the Electron Paramagnetic Resonance Center, The Johns Hopkins University School of Medicine, Baltimore, MD, 21224, USA
SOURCE: Antioxidants & Redox Signaling (2001), 3(1), 11-22
CODEN: ARSIF2; ISSN: 1523-0864
PUBLISHER: Mary Ann Liebert
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 44 refs. Alterations in the production of nitric oxide (NO·) are a critical factor in the injury that occurs in ischemic and reperfused myocardium; however, controversy remains regarding the alterations in NO· that occur and how these alterations cause tissue injury. As superoxide generation occurs during the early period of reperfusion, the cytotoxic oxidant peroxynitrite (ONOO-) could be formed; however, questions remain regarding ONOO- formation and its role in postischemic injury. ESR spin trapping studies, using the NO· trap Fe2+-N-methyl-D-glucamine dithiocarbamate (Fe-MGD), and chemiluminescence studies, using the enhancer luminol, have been performed to measure the magnitude and time course of NO· and ONOO- formation in the normal and postischemic heart. Isolated rat hearts were subjected to control

perfusion, or ischemia followed by reperfusion in the presence of Fe-MGD with ESR measurements performed on the effluent from these hearts. Whereas only trace signals were present prior to ischemia, prominent NO· adduct signals were seen during the first 2 min of reflow. The reperfusion associated increase in these NO· signals was abolished by nitric oxide synthase inhibition. In hearts perfused with luminol to detect ONOO- formation, a similar marked increase was seen during the first 2 min of reperfusion that was blocked by nitric oxide synthase inhibitors and by superoxide dismutase. Either NG-nitro-L-arginine Me ester or superoxide dismutase treatment resulted in more than twofold higher recovery of contractile function than in untreated hearts. Immunohistol. studies demonstrated that the ONOO--mediated nitration product nitrotyrosine was formed in postischemic hearts, but not in normally perfused controls. Thus, NO· formation is increased during the early period of reperfusion and reacts with superoxide to form ONOO-, which results in protein nitration and myocardial injury.

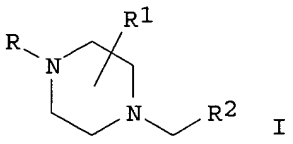
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L95 ANSWER 32 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:222006 HCAPLUS
DOCUMENT NUMBER: 134:252354
TITLE: Preparation of N-benzylpiperazines as antiinflammatory agents
INVENTOR(S): Bauman, John G.; Buckman, Brad O.; Ghannam, Ameen F.; Hesselgesser, Joseph E.; Horuk, Richard; Islam, Imadul; Liang, Meina; May, Karen B.; Monahan, Sean D.; Morrissey, Michael M.; Ng, Howard P.; **Wei, Guo Ping**; Xu, Wei; Zheng, Wei
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: U.S., 87 pp., Cont.-in-part of U.S. Ser. No. 873,599, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

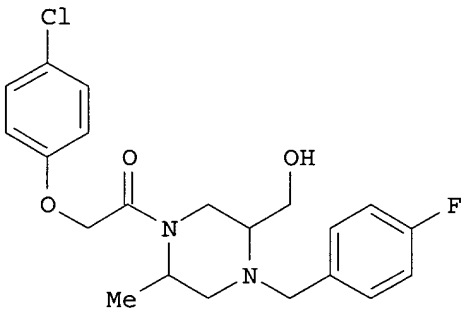
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6207665	B1	20010327	US 1998-94397	19980609
CA 2293382	AA	19981217	CA 1998-2293382	19980611
AU 9886258	A1	19981230	AU 1998-86258	19980611
AU 735462	B2	20010712		
EP 988292	A2	20000329	EP 1998-937467	19980611
EP 988292	B1	20030212		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
EE 9900565	A	20000615	EE 1999-565	19980611
EE 4056	B1	20030616		
TR 9903034	T2	20000621	TR 1999-9903034	19980611
JP 2002503239	T2	20020129	JP 1999-501611	19980611
EP 1254899	A2	20021106	EP 2002-90193	19980611
EP 1254899	A3	20030219		
EP 1254899	B1	20050525		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
AT 232522	E	20030215	AT 1998-937467	19980611
EE 200200682	A	20030415	EE 2002-200200682	19980611
EE 200200683	A	20030415	EE 2002-200200683	19980611

EE 200200684	A	20030415	EE 2002-200200684	19980611
ES 2191320	T3	20030901	ES 1998-937467	19980611
IL 132398	A1	20040831	IL 1998-132398	19980611
AT 296292	E	20050615	AT 2002-90193	19980611
NO 9906068	A	20000211	NO 1999-6068	19991209
MX 9911506	A	20000430	MX 1999-11506	19991210
US 6541476	B1	20030401	US 2000-713606	20001114
US 6534509	B1	20030318	US 2000-713881	20001115
US 6573266	B1	20030603	US 2000-714937	20001116
US 2002177598	A1	20021128	US 2000-726808	20001129
US 6555537	B2	20030429		
US 2003139425	A1	20030724	US 2003-347530	20030117
US 2003158205	A1	20030821	US 2003-347529	20030117
NO 2003001373	A	20000211	NO 2003-1373	20030326
PRIORITY APPLN. INFO.:			US 1997-873599	B2 19970612
			US 1998-94397	A 19980609
			EP 1998-937467	A3 19980611
			WO 1998-EP3503	W 19980611
			US 2000-714937	A3 20001116
			US 2000-726808	A1 20001129

OTHER SOURCE(S): MARPAT 134:252354
GI



I



II

AB Title compds. [I; R = R3Z3Z2Z1; R1 = ≥1 of halo, alkyl, aryl, etc.; R2 = (un)substituted Ph; R3 = (un)substituted carbocyclic ring system (sic) or (un)substituted heterocyclic ring system (sic); Z1 = bond, CH2, CO, etc.; Z2 = alkylene or alkylidene; Z3 = bond, O, CH2, (alkyl)imino, etc.] were prepared as chemokine inhibitors (no data). Thus, (2R,5S)-1-(4-fluorobenzyl)-2-hydroxymethyl-5-methylpiperazine was N-acylated by 4-ClC6H4OCH2COCl to give title compound (R,R)-II.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L95 ANSWER 33 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:777035 HCAPLUS
DOCUMENT NUMBER: 134:999
TITLE: transcription factor ets-2 is a target for an Akt (protein kinase B)/jun N-terminal kinase signaling pathway in macrophages of motheaten-viable mutant mice
AUTHOR(S): Smith, James L.; Schaffner, Alicia E.; Hofmeister, Joseph K.; Hartman, Matthew; **Wei, Guo**; Forsthoefel, David; Hume, David A.; Ostrowski, Michael C.
CORPORATE SOURCE: Department of Molecular Genetics and the Comprehensive Cancer Center, Ohio State University, Columbus, OH,

43210, USA
SOURCE: Molecular and Cellular Biology (2000), 20(21), 8026-8034
CODEN: MCEBD4; ISSN: 0270-7306
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The transcription factor ets-2 was phosphorylated at residue threonine 72 in a colony-stimulating factor 1 (CSF-1)- and mitogen-activated protein kinase-independent manner in macrophages isolated from motheaten-viable (me-v) mice. The CSF-1 and ets-2 target genes coding for Bcl-x, urokinase plasminogen activator, and scavenger receptor were also expressed at high levels independent of CSF-1 addition to me-v cells. Akt (protein kinase B) was constitutively active in me-v macrophages, and an Akt immunoppt. catalyzed phosphorylation of ets-2 at threonine 72. The p54 isoform of c-jun N-terminal kinase-stress-activated kinase (JNK-SAPK) coimmunopptd. with Akt from me-v macrophages, and treatment of me-v cells with the specific phosphatidylinositol 3-kinase inhibitor LY294002 decreased cell survival, Akt and JNK kinase activities, ets-2 phosphorylation, and Bcl-x mRNA expression. Therefore, ets-2 is a target for phosphatidylinositol 3-kinase-Akt-JNK action, and the JNK p54 isoform is an ets-2 kinase in macrophages. Constitutive ets-2 activity may contribute to the pathol. of me-v mice by increasing expression of genes like the Bcl-x gene that promote macrophage survival.
REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L95 ANSWER 34 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:617494 HCAPLUS
DOCUMENT NUMBER: 134:113897
TITLE: Prognostic impact of INK4A deletion in Ewing sarcoma
AUTHOR(S): **Wei, Guo**; Antonescu, Cristina R.; de Alava, Enrique; Leung, Denis; Huvos, Andrew G.; Meyers, Paul A.; Healey, John H.; Ladanyi, Marc
CORPORATE SOURCE: Department of Orthopaedic Surgery, People's Hospital, Beijing, Peop. Rep. China
SOURCE: Cancer (New York) (2000), 89(4), 793-799
CODEN: CANCAR; ISSN: 0008-543X
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The primary genetic alteration in > 95% of Ewing sarcomas (ES) is a specific fusion of EWS with FLII or ERG. Secondary genetic alterations possibly involved in progression of ES are not well understood. A recent study found loss of the neg. cell cycle regulator gene INK4A in 8 of 27 ES samples (30%). To confirm these findings and evaluare their prognostic significance, the authors studied INK4A deletion in 41 ES samples from 39 patients. Using Southern blot anal. with an INK4A p16 cDNA probe, the intensity of the INK4A bands in ES DNA samples was normalized to that of a control probe and compared with nondeleted control DNA; > 50% signal reduction was scored as evidence of deletion. All ES tumor DNA samples previously were confirmed to have EWS rearrangements on the same Southern blots, using a cDNA probe spanning the EWS breakpoint region. Tumors from 7 patients (18%) showed INK4A deletion independent of disease stage (localized or metastatic) or sample source (primary tumor or metastasis). INK4A was a strong neg. factor for disease specific survival in univariate anal. (P = 0.001) and in multivariate anal. including stage (relative risk = 6; P = 0.001). INK4A deletions appear to be the most frequent secondary mol. genetic alteration found to date in ES. Their possible clin. usefulness in identifying a subset of ES patients with poor prognosis

merits systematic prospective anal.
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L95 ANSWER 35 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:551005 HCAPLUS
DOCUMENT NUMBER: 134:13200
TITLE: Myocardial postischemic injury is reduced by polyADPribose polymerase-1 gene disruption
AUTHOR(S): Pieper, Andrew A.; Walles, Thorsten; **Wei, Guo**; Clements, Emily E.; Verma, Ajay; Snyder, Solomon H.; Zweier, Jay L.
CORPORATE SOURCE: Departments of Neuroscience, Pharmacology & Molecular Science, The Johns Hopkins University School of Medicine, Baltimore, MD, 21224, USA
SOURCE: Molecular Medicine (New York) (2000), 6(4), 271-282
CODEN: MOMEF3; ISSN: 1076-1551
PUBLISHER: Johns Hopkins University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB PolyADPribose polymerase (PARP) is activated by DNA strand breaks to catalyze the addition of ADPribose groups to nuclear proteins, especially PARP-1.
Excessive polyADPribosylation leads to cell death through depletion of NAD+ and ATP. In vivo PARP activation in heart tissue slices was assayed through conversion of [33P]NAD+ into polyADPribose (PAR) following ischemia-reperfusion (I/R) and also monitored by immunohistochem. staining for PAR. Cardiac contractility, nitric oxide (NO), reactive oxygen species (ROS), NAD+ and ATP levels were examined in wild type (WT) and in PARP-1 gene-deleted (PARP-1-/-) isolated, perfused mouse hearts. Myocardial infarct size was assessed following coronary artery occlusion in rats treated with PARP inhibitors. Ischemia-reperfusion (I/R) augmented formation of nitric oxide, oxygen free radicals and PARP activity. I/R induced decreases in cardiac contractility and NAD+ levels were attenuated in PARP-1-/- mouse hearts. PARP inhibitors reduced myocardial infarct size in rats. Residual polyADPribosylation in PARP-1-/- hearts may reflect alternative forms of PARP. PolyADPribosylation from PARP-1 and other sources of enzymic PAR synthesis is associated with cardiac damage following myocardial ischemia. PARP inhibitors may have therapeutic utility in myocardial disease.
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L95 ANSWER 36 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:217806 HCAPLUS
DOCUMENT NUMBER: 133:40083
TITLE: Study and application on polarographic catalytic wave of human serum albumin in the presence of KIO3
AUTHOR(S): **Wei, Guo**; Yani, Yang; Junfeng, Song
CORPORATE SOURCE: Department of Chemistry, Northwest University, Xi'an, 710069, Peop. Rep. China
SOURCE: Analytical Letters (2000), 33(5), 847-859
CODEN: ANALBP; ISSN: 0003-2719
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A polarog. catalytic wave of human serum albumin (HSA) in the presence of KIO3 was reported. In 0.1 M NaAc.apprx.HAc buffer (pH4.7) solution, a reduction
wave of HSA with peak potential -0.60 V (vs, Ag/AgCl) resulted from the

reduction of five disulfide linkages to sulfhydryl group. In the presence of KIO3, HSA yielded a polarog. catalytic wave at the original potential due to reduction and regeneration of these disulfide linkages. The catalytic wave can be used to determine trace of HSA. In the 0.1 M HAc.apprx.NaAc (pH4.7±0.2) .apprx.1+10-3 M KIO3 solution, the peak current was linearly proportional to HSA concentration in the range of 1.5+10-7.apprx.7.5+10-7 M. The catalytic wave improved two orders of magnitude in sensitivity compared with corresponding reduction wave.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L95 ANSWER 37 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:165156 HCAPLUS
DOCUMENT NUMBER: 132:254769
TITLE: Thermal decomposition mechanism of barium titanate nanoparticle synthesis
AUTHOR(S): Li, Qinglian; Chen, Shoutian; Yao, Pu; **Wei, Guo**; Qu, Yonghe
CORPORATE SOURCE: State Key Laboratory of Electrical Insulation for Power Equipment, Xi'an Jiaotong University, Xi'an, 710049, Peop. Rep. China
SOURCE: Wuli Huaxue Xuebao (2000), 16(2), 170-174
CODEN: WHXUEU; ISSN: 1000-6818
PUBLISHER: Beijing Daxue Chubanshe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB Thermal decomposition reaction mechanism of the precursor gel made by sol-gel process for nano-crystalline BaTiO3 was studied by TG-DTG and FTIR techniques. The reaction proceeded in three stages: solvents removing, organic ligands decomposing, and amorphous solid BaTiO3 forming. The differential and integral mechanism functions and activation energy for the third stage were obtained by calcn. and comparison.

L95 ANSWER 38 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:107269 HCAPLUS
DOCUMENT NUMBER: 132:123682
TITLE: Preparation and application of modified polysulfone super-filter membrane
INVENTOR(S): Shang, Zhenhua; **Wei, Guo**; Yu, Yinian; Zhou, Liangmo
PATENT ASSIGNEE(S): Dalian Inst. of Chemicophysics, Chinese Academy of Sciences, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 8 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1125635	A	19960703	CN 1994-112724	19941228
CN 1059356	B	20001213		
PRIORITY APPLN. INFO.:			CN 1994-112724	19941228

AB The membrane of modified polysulfone containing 4-aminophenylamino or 4-aminobenzoyl group is prepared by acylating polysulfone with 4-nitrobenzoyl chloride and AlCl3 as catalyst at 60-80°, and aminating with hydrazine at 40-60°. The membrane may be prepared by chloromethylating with chloromethyl ether and AlCl3 as catalyst at 20-30°, and aminating with 1,4-benzenediamine at 55-65°.

The affinity membrane is prepared by fixing trypsin with the membrane by crosslinking in presence of glutaraldehyde or diazotizing at 0-4°. The affinity membrane is used for separation and purification of trypsin inhibitor.

L95 ANSWER 39 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:703503 HCAPLUS
DOCUMENT NUMBER: 132:18731
TITLE: NBPA: a cerebral ischemic protective agent
AUTHOR(S): Zhang, Juntian; Peng, Xinqi; **Wei, Guo**; Su, Dan
CORPORATE SOURCE: Institute of Materia Medica, Chinese Academy of Medical Sciences and Beijing Union Medical College, Beijing, Peop. Rep. China
SOURCE: Clinical and Experimental Pharmacology and Physiology (1999), 26(10), 845-846
CODEN: CEXPB9; ISSN: 0305-1870
PUBLISHER: Blackwell Science Asia Pty Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB NBPA is a derivative of 3-n-butylpathalide isolated from Apium granolens Linn. At concns. ranging from 6 + 10-6 to 10-6 mol/L, NBPA inhibited the L-type calcium current in guinea-pig myocardial cells and cultured human neuroblastoma cells. At 10-6 mol/L, NBPA markedly inhibited calcium-dependent and -independent release of glutamate from synaptosomes. The [31P] NMR spectrum has shown that pretreatment with NBPA at 15 mg/kg, i.p., improved energy metabolism In situ hybridization has shown that 10 and 20 mg/kg, i.p., NBPA prior to cerebral artery occlusion can accelerate the expression of heat shock protein 70 mRNA and inhibit c-fos mRNA expression. It has been shown that NBPA decreases the nitric oxide content and bc nitric oxide synthase (NOS) activity in the global cerebral ischemia-reperfusion model in rats. In addition, it has been shown that NBPA significantly inhibits the expression of inducible NOS protein.
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L95 ANSWER 40 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:386761 HCAPLUS
DOCUMENT NUMBER: 131:123769
TITLE: Design of ZnO/SiO2/Si monolithic integrated programmable SAW filter
AUTHOR(S): Zhu, Dazhong; Han, Xiaoxia; **Wei, Guo**
CORPORATE SOURCE: Department of Information and Electronic Engineering, Zhejiang University, Hangzhou, 310027, Peop. Rep. China
SOURCE: Proceedings - International Conference on Solid-State and Integrated Circuit Technology, 5th, Beijing, Oct. 21-23, 1998 (1998), 826-829. Editor(s): Zhang, Min; Tu, King Ning. Institute of Electrical and Electronics Engineers: New York, N. Y.
CODEN: 67TKAC
DOCUMENT TYPE: Conference
LANGUAGE: English
AB In this paper, the design of a ZnO/SiO2/Si monolithic integrated programmable SAW filter is suggested. The input SAW interdigital transducer (IDT) and tap delay lines (TDL) are fabricated on the ZnO/SiO2 structure. NMOS-DMOS sampling, weighting, controlling, and summing integrated circuit are designed compatibly in the SiO2/Si structure. This integrated circuit can control the IDT and TDL by programmable weighting the signal to realize the shift of the central frequency of the bandpass

of this SAW filter.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L95 ANSWER 41 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:280082 HCAPLUS
DOCUMENT NUMBER: 131:113577
TITLE: Application of automated blood culture system for raising positive rate
AUTHOR(S): Jiang, Yanqun; **Wei, Guo**; Ni, Yuxing
CORPORATE SOURCE: Shanghai Sixth People's Hospital, Shanghai, 200233, Peop. Rep. China
SOURCE: Zhonghua Yixue Jianyan Zazhi (1999), 22(2), 71-73
CODEN: CHCCDO; ISSN: 0253-973X
PUBLISHER: Zhonghua Yixuehui Zazhishe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The pos. detection rate of blood culture was raised to diagnose pathogens rapidly. A total of 1 000 samples of blood and body fluid were detected by BACTEC-9120 automated blood culture system with standard aerobic vials, aerobic vials, and peds plus vials. 149 Strains (14.9%) were isolated, 40(4.0%) were false pos., and 9(0.9%) were contaminated. A pos. rate of 52.6% was detected in 24 h, and 71.8% in 48 h. 110(11.0%) Strains were taken from blood and 36 strains from body fluid. These isolates included 43 species. The rate of septicemia from coagulase-neg. staphylococcus were high to 41.6%, and 65.7% of septicemia cases were secondary to a focal bacterial infection or secondary to an underlying disease with impaired defense-mechanisms. The pos. detection rate was raised and the detection time was reduced by BACTEC-9120. Most of septicemia are caused by conditional pathogen.

L95 ANSWER 42 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:80169 HCAPLUS
DOCUMENT NUMBER: 130:253489
TITLE: Effect of concentration and charging methods of n-dodecyl mercaptan on MW, MWD and branching of polychloroprene rubber
AUTHOR(S): Hong, Yao; Fu, Zhifeng; **Wei, Guo**; Xueyi, Zhang
CORPORATE SOURCE: College of Materials Science and Engineering, Beijing University of Chemical Technology, Beijing, 100029, Peop. Rep. China
SOURCE: Beijing Huagong Daxue Xuebao, Ziran Kexueban (1998), 25(4), 23-27,32
CODEN: BHDKFA; ISSN: 1007-2640
PUBLISHER: Beijing Huagong Daxue Xuebao Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The emulsion polymerization of chloroprene was conducted at 10° with n-dodecyl mercaptan as chain transfer agent, potassium salt of disproportionated rosin acid as emulsifier and potassium persulfate/sodium sulfite/sodium anthraquinone-2-sulfonate as redox initiator. The effects of mercaptan concentration and its charging methods, and monomer conversion on mol. weight (MW) and its distribution (MWD), and branching content of polychloroprene were investigated. High mol. weight polychloroprene with narrow mol. weight distribution and low branching extent could be obtained when mercaptan was charged in two increments at appropriate monomer conversion.

L95 ANSWER 43 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:13149 HCAPLUS
DOCUMENT NUMBER: 130:235580
TITLE: CDK4 gene amplification in osteosarcoma: reciprocal relationship with INK4A gene alterations and mapping of 12q13 amplicons
AUTHOR(S): **Wei, Guo**; Lonardo, Fulvio; Ueda, Takafumi; Kim, Tonia; Huvos, Andrew G.; Healey, John H.; Ladanyi, Marc
CORPORATE SOURCE: Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY, USA
SOURCE: International Journal of Cancer (1999), 80(2), 199-204
CODEN: IJCNAW; ISSN: 0020-7136
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The INK4A gene, localized to human chromosome 9p21, encodes p16INK4A, a tumor suppressor that functions at least in part through the inhibition of CDK4, a cyclin-dependent kinase encoded by a gene at 12q13. To examine INK4A gene alterations in uncultured samples of osteosarcoma and the relationship between INK4A and CDK4 alterations, we analyzed the INK4A and CDK4 genes in 87 specimens from 79 patients. INK4A deletion and CDK4 gene amplification were determined by quant. Southern blot anal. INK4A exon 2 was screened for mutation by polymerase chain reaction and single-strand conformational polymorphism anal. Methylation at the CpG island in INK4A, associated with loss of p16INK4A expression, was assessed by Southern blot anal. using methylation-sensitive restriction enzymes. INK4A deletion (4/55) or rearrangement (1/55) was found in 5 of 55 cases. No INK4A exon 2 point mutations and methylation were detected. CDK4 gene amplification was found in 6 of 67 samples, but not in tumors with INK4A alteration. Amplification anal. of other genes at 12q13 (GLI, CHOP, HMGI-C and MDM2) in these 6 cases supports the view that CDK4 and MDM2 are independent targets for amplification, with variable amplification of the intervening region containing HMGI-C. Of 46 patients studied for both INK4A alterations and CDK4 amplification, the tumors in 22% contained one or the other. The prevalence of these alterations, in conjunction with the reported inactivation of RB in up to 80% of cases, suggests that genetic lesions deregulating the G1, to S cell cycle checkpoint may be an almost constant feature in the pathogenesis of osteosarcoma.
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

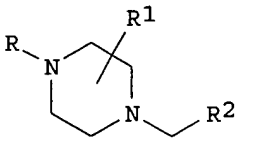
L95 ANSWER 44 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:7977 HCAPLUS
DOCUMENT NUMBER: 130:66509
TITLE: Preparation of N-benzylpiperazines as antiinflammatory agents
INVENTOR(S): Bauman, John G.; Buckman, Brad O.; Ghannam, Ameen F.; Hesselgesser, Joseph E.; Horuk, Richard; Islam, Imadul; Liang, Meina; May, Karen B.; Monahan, Sean D.; Morissey, Michael M.; Ng, Howard P.; **Wei, Guo Ping**; Xu, Wei; Zheng, Wei
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 309 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

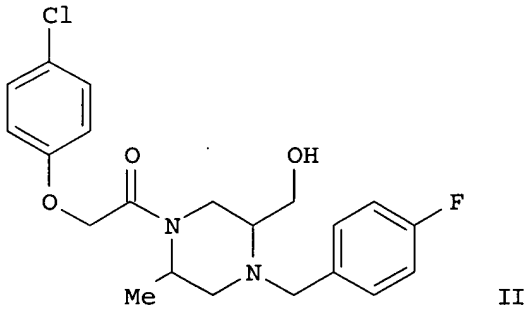
WO 9856771	A2	19981217	WO 1998-EP3503	19980611
WO 9856771	A3	19990311		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2293382	AA	19981217	CA 1998-2293382	19980611
AU 9886258	A1	19981230	AU 1998-86258	19980611
AU 735462	B2	20010712		
EP 988292	A2	20000329	EP 1998-937467	19980611
EP 988292	B1	20030212		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
EE 9900565	A	20000615	EE 1999-565	19980611
EE 4056	B1	20030616		
JP 2002503239	T2	20020129	JP 1999-501611	19980611
AT 232522	E	20030215	AT 1998-937467	19980611
EE 200200682	A	20030415	EE 2002-200200682	19980611
EE 200200683	A	20030415	EE 2002-200200683	19980611
EE 200200684	A	20030415	EE 2002-200200684	19980611
IL 132398	A1	20040831	IL 1998-132398	19980611
NO 9906068	A	20000211	NO 1999-6068	19991209
MX 9911506	A	20000430	MX 1999-11506	19991210
NO 2003001373	A	20000211	NO 2003-1373	20030326
PRIORITY APPLN. INFO.:			US 1997-873599 A	19970612
			US 1998-94397 A	19980609
			WO 1998-EP3503 W	19980611

OTHER SOURCE(S): MARPAT 130:66509

GI



I



II

AB Title compds. [I; R = R3Z3Z2Z1; R1 = ≥1 of halo, alkyl, aryl, etc.; R2 = (un)substituted Ph; R3 = (un)substituted carbocyclic ring system (sic) or (un)substituted heterocyclic ring system (sic); Z1 = bond, CH2, CO, etc.; Z2 = alkylene or alkylidene; Z3 = bind, O, CH2, (alkyl)imino, etc.] were prepared as chemokine inhibitors (no data). Thus, (2R,5S)-1-(4-fluorobenzyl)-2-hydroxymethyl-5-methylpiperazine was N-acylated by 4-ClC6H4OCH2COCl to give title compound (R,R)-II.

L95 ANSWER 45 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:489768 HCAPLUS
DOCUMENT NUMBER: 129:288296
TITLE: Cerebral ischemia injury and programmed cell death
AUTHOR(S): **Wei, Guo**; Zhang, Juntian
CORPORATE SOURCE: Institute of Materia Medica, Chinese Academy of Medical Sciences, Beijing, 100050, Peop. Rep. China
SOURCE: Shengli Kexue Jinzhan (1998), 29(1), 45-48
CODEN: SLKHA8; ISSN: 0559-7765
PUBLISHER: Zhongguo Shengli Xuehui
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review with 10 refs. on (1) programmed cell death (PCD) evolved in pathophysiol. course after ischemia; delayed injury of neuron and PCD; (3) function of PCD in ischemia; (4) mechanisms of PCD after ischemia. The increase of calcium influx, production of nitric oxide, lipid peroxidn. and expression of P53 play an important role in PCD.

L95 ANSWER 46 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:433041 HCAPLUS
DOCUMENT NUMBER: 129:214703
TITLE: Protective effect of nerve growth factor on peripheral nerve injury
AUTHOR(S): Wu, Junfang; Qu, Zhiwei; **Wei, Guo**; Zhang, Juntian
CORPORATE SOURCE: Institute of Materia Medica, Chinese Academy Of Medical Sciences, Beijing, 100050, Peop. Rep. China
SOURCE: Yaoxue Xuebao (1998), 33(3), 180-183
CODEN: YHHPAL; ISSN: 0513-4870
PUBLISHER: Chinese Academy of Medical Sciences, Institute of Materia Media
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB Peripheral sympathetic nerve injury induced by i.p. injection of 6-hydrodopamine (6HD); mech. injured ulnar nerve; and serum free cultured dorsal root ganglion of newborn rat in vitro were used as models to study the protective effect of nerve growth factor (NGF) on peripheral nerve injury. NGF dose dependently raised the residue norepinephrine content in submandibular gland after i.p. injection of 6HD; preserved cell nos. of C7 and T1 dorsal root ganglia after mech. injured ulnar nerve; and dramatically promoted the growth of neuronal projections in serum free cultured dorsal root ganglion. The results suggest that NGF is protective on peripheral nerve injury and neurotropic on sensory neurons.

L95 ANSWER 47 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:433009 HCAPLUS
DOCUMENT NUMBER: 129:255413
TITLE: Effect of neurotropin on brain edema induced by permanent focal cerebral ischemia in rats and collateral ventricular injection of carrageenan in mice
AUTHOR(S): Qu, Zhiwei; **Wei, Guo**; Zgang, Liying; Wu, Junfang; Zhang, Juntian
CORPORATE SOURCE: Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, 100050, Peop. Rep. China
SOURCE: Yaoxue Xuebao (1998), 33(2), 98-101
CODEN: YHHPAL; ISSN: 0513-4870
PUBLISHER: Chinese Academy of Medical Sciences, Institute of Materia Media

DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB Brain edema models of rats induced by permanent ligation of middle cerebral artery, and in mice induced by lateral cerebral ventricular injection of carrageenan were used to study the effect of neurotropin. Neurotropin effectively reduced the water content of the exptl. animals via i.v. administration. The results suggest that the mechanism of neurotropin reduces ischemic brain edema might be mediated via the inhibition of kallikrein-kinin system.

L95 ANSWER 48 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:400595 HCAPLUS
DOCUMENT NUMBER: 129:144656
TITLE: Identification and characterization of small molecule functional antagonists of the CCR1 chemokine receptor
AUTHOR(S): Hesselgesser, Joseph; Ng, Howard P.; Liang, Meina; Zheng, Wei; May, Karen; Bauman, John G.; Monahan, Sean; Islam, Imadul; **Wei, Guo Ping**; Ghannam, Ameen; Taub, Dennis D.; Rosser, Mary; Snider, R. Michael; Morrissey, Michael M.; Perez, H. Daniel; Horuk, Richard
CORPORATE SOURCE: Department of Immunology, Berlex BioSciences, Richmond, CA, 94806, USA
SOURCE: Journal of Biological Chemistry (1998), 273(25), 15687-15692
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The CC chemokines macrophage inflammatory protein-1α (MIP-1α) and RANTES (regulated on activation normal T cell expressed) have been implicated in rheumatoid arthritis and multiple sclerosis. Since their effects are mediated through the CCR1 chemokine receptor, we set up a small mol. CCR1 antagonist program to search for inhibitors. Through high capacity screening we discovered a number of 4-hydroxypiperidine compds. with CCR1 antagonist activity and report their synthesis and in vitro pharmacol. here. Scatchard anal. of the competition binding data revealed that the compds. had Ki values ranging from 40 to 4000 nM. The pharmacol. profile of the most potent member of this series, (2,2-diphenyl-5-(4-chlorophenyl)piperidinlyl)valeronitrite (I), was further evaluated. Compound I showed concentration-dependent inhibition of MIP-1α-induced extracellular acidification and Ca2+ mobilization demonstrating functional antagonism. When given alone, the compound did not elicit any responses, indicating the absence of intrinsic agonist activity. Compound I inhibited MIP-1α- and RANTES-induced migration in peripheral blood mononuclear cells in a dose-responsive manner. Selectivity testing against a panel of seven transmembrane domain receptors indicated that compound I is inactive on a number of receptors at concns. up to 10 μM. This is the first description of CCR1 receptor antagonists that may be useful in the treatment of chronic inflammatory diseases involving MIP-1α, RANTES, and CCR1.
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L95 ANSWER 49 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:49993 HCAPLUS
DOCUMENT NUMBER: 128:114904
TITLE: Solid phase synthesis of benzimidazolones
AUTHOR(S): **Wei, Guo Ping**; Phillips, Gary B.

CORPORATE SOURCE: Berlex Biosciences, Richmond, CA, 94804, USA
SOURCE: Tetrahedron Letters (1998), 39(3/4), 179-182
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 128:114904
AB An efficient solid phase synthesis of benzimidazol-2-one-5-carboxylic acids is described. Polymer bound o-fluoronitro aromatic compound was treated with an amine to give o-nitroaniline derivs. Reduction of the latter with SnCl2 followed by cyclization with DSC gave benzimidazolones. Reaction with NaH and an alkyl bromide followed by cleavage with TFA gave benzimidazol-2-one-5-carboxylic acids. A library of 13 benzimidazolones has been prepared in three steps in 90-100 % crude yield and 91-95 % purity.
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L95 ANSWER 50 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:766523 HCAPLUS
DOCUMENT NUMBER: 128:4400
TITLE: Ion exchange technique for extraction of boron
AUTHOR(S): Xiao, Yingkai; Xiao, Yun; Swihart, G. H.; **Wei, Guo**
CORPORATE SOURCE: Qinghai Inst. Salt Lakes, Academia Sinica, Xining, 810008, Peop. Rep. China
SOURCE: Fenxi Huaxue (1997), 25(11), 1359
CODEN: FHHHDT; ISSN: 0253-3820
PUBLISHER: Zhongguo Huaxuehui "Fenxi Huaxue" Bianji Weiyuanhui
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB Effects of pH, volume, and salt concentration of solution of ion exchange on B adsorption of ion exchange resin Amberlite IRA-743 were studied. An improved method for B elution was proposed.

L95 ANSWER 51 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:763260 HCAPLUS
DOCUMENT NUMBER: 128:57264
TITLE: Development of brain edema in hypertensive and normotensive rats 24 hours after focal cerebral ischemia and effect of 764-3 on it
AUTHOR(S): **Wei, Guo**; Chen, Feisong; Yan, Huijin; Zhao, Huimin; Wei, Beihai
CORPORATE SOURCE: Dep. Physiology, Peking Union Med. College, Beijing, 100005, Peop. Rep. China
SOURCE: Zhongguo Yaolixue Tongbao (1997), 13(2), 129-132
CODEN: ZYTOE8; ISSN: 1001-1978
PUBLISHER: Anhui Yike Daxue Linchuan Yaoli Yanjiuso
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The effect of 764-3 on the injury of cerebral ischemia in normotensive and renal hypertensive rats was observed The cortex, caudate and hippocampus developed edema in normotensive rats and amygdala developed edema in hypertensive rats. The content of malondialdehyde and cerebral vascular permeability increased not only in normotensive rats but also in hypertensive rats. 764-3 Administration ameliorated 3 abnormalities except the increased cerebral vascular permeability in hypertensive rats. The results suggest that 764-3 had some protect effects on cerebral ischemia injury in normotensive and renal hypertensive rats.

L95 ANSWER 52 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN

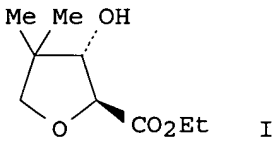
ACCESSION NUMBER: 1997:444496 HCAPLUS
DOCUMENT NUMBER: 127:156577
TITLE: Effect of tetrandrine on proto-oncogene c-fos expression in rat cerebrum
AUTHOR(S): Che, Jian-Tu; Zhang, Jun-Tian; Qu, Zhi-Wei; **Wei, Guo**
CORPORATE SOURCE: Institute Materia Medica, Chinese Academy Medical Sciences & Peking Union Medical College, Beijing, 100050, Peop. Rep. China
SOURCE: Zhongguo Yaoli Xuebao (1997), 18(4), 371-373
CODEN: CYLPDN; ISSN: 0253-9756
PUBLISHER: Kexue
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The aim was to detect the effect of tetrandrine (Tet) on c-fos gene expression in cerebrum induced by lindane, a neurotoxicant which activates Ca2+ channels. Northern and dot blotting, dual wavelength thin layer chromatog. scanner, were used in this study. Lindane 30 mg·kg-1 given by intragastric gavage (ig) increased the expression of c-fos gene to 146 mm2 in rat cerebrum 1 h after treatment. Tet 1, 2, and 4 mg·kg-1 given by ig 30 min prior to lindane reduced c-fos gene expression in a concentration-dependent manner. Expressed genes reached only 86, 40, and 39 mm2, resp. Tet inhibited c-fos gene expression in rat cerebrum induced by the Ca2+ agonist-lindane.
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L95 ANSWER 53 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:349992 HCAPLUS
DOCUMENT NUMBER: 127:7830
TITLE: Simulation of necking development and fracture of superplasticity under uniaxial tension
AUTHOR(S): Chen, Jiwei; **Wei, Guo**; Hu, Ping; Lian, Jianshe
CORPORATE SOURCE: Jilin University of Technology, Changchun, 130025, Peop. Rep. China
SOURCE: Proceedings of the Asia-Oceania International Symposium on Plasticity, 1st, Beijing, Aug. 16-19, 1993 (1994), Meeting Date 1993, 198-205. Editor(s): Wang, Tzuchiang; Xu, Bingye. Peking University Press: Beijing, Peop. Rep. China.
CODEN: 64KYAM
DOCUMENT TYPE: Conference
LANGUAGE: English
AB A phenomenol. model including the two-stage variation of cavity growth with strain was proposed for several superplastic alloys. The simulation of necking development and elongation to fracture is realized for three superplastic alloys (Zn-22%Al, Coronze 638 and Ly12cz).

L95 ANSWER 54 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:95246 HCAPLUS
DOCUMENT NUMBER: 126:154679
TITLE: Fluormetric method for determination of nitric oxide and nitric oxide synthetase in rat brain
AUTHOR(S): **Wei, Guo**; Zhang, Juntian
CORPORATE SOURCE: Inst. Pharmacol. Toxicol., Chinese Acad. Medical Scis., Beijing, 100050, Peop. Rep. China
SOURCE: Yaoxue Xuebao (1996), 31(7), 530-534
CODEN: YHHPAL; ISSN: 0513-4870

PUBLISHER: Chinese Academy of Medical Sciences, Institute of Materia Media
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB Based on the inner filter effect of N-acetylcysteine nitrosothiol, the reaction product of N-acetylcysteine and nitric oxide, overlapping the absorption of quinine sulfate, a fluormetric method of the determination of nitric oxide and nitric oxide synthetase in rat brain homogenates was developed. Experiment demonstrated neither N-acetylcysteine nor nitric oxide but N-acetylcysteine nitrosothiol exhibited the inner filter effect; at pH 7.4 the determination limit is 3 + 10-8 mol/L. The calibration curve for nitric oxide and nitric oxide synthetase were plotted by concns. of N-acetylcysteine nitrosothiol against the fluorescent intensity and changes of fluorescent intensity. The method determined nitric oxide content was 477.7 ± 93 pmol/mg protein and the nitric oxide synthetase activity was 4.86 ± 0.79 pmol/min/mg protein in 250-350 g male Wistar rat brain. The results suggest that the method is specific and simple, and dynamic monitoring of nitric oxide synthetase activity is possible.

L95 ANSWER 55 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:683345 HCAPLUS
DOCUMENT NUMBER: 123:198535
TITLE: Stereoselective synthesis of substituted tetrahydrofurans via Lewis acid promoted reaction of β-benzyloxyaldehydes and ethyl diazoacetate.
AUTHOR(S): Angle, Steven R.; **Wei, Guo Ping**; Ko, Young Kwan; Kubo, Keiji
CORPORATE SOURCE: Department of Chemistry, University of California, Riverside, CA, 92521-0403, USA
SOURCE: Journal of the American Chemical Society (1995), 117(30), 8041-2
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 123:198535
GI



I

AB The title reaction is mediated by several different Lewis acids; 0.5 equivalent SnCl4 gave the highest yields. Et diazoacetate and SnCl4 were sequentially added to a -78° solution of 4-MeOC6H4CH2OCH2CMe2CHO in CH2Cl2 to give 84% tetrahydrofuran (I).

L95 ANSWER 56 OF 56 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:144824 HCAPLUS
DOCUMENT NUMBER: 120:144824
TITLE: A study of atomic time scale stability
AUTHOR(S): **Wei, Guo**
CORPORATE SOURCE: Shaanxi Obs., Acad. Sin., Lintong, 710600, Peop. Rep. China

SOURCE: Science in China, Series A: Mathematics, Physics, Astronomy & Technological Sciences (1993), 36(6), 729-37
CODEN: SCASEY; ISSN: 1001-6511
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The principle of System Clock in time scale is presented and some related propositions are proved based on the anal. of atomic clock noise characteristics. The purpose is to provide a new theor. frame for the anal. of time scale algorithm. Under the principle, the classical weighted average methodol. is discussed and some drawbacks of the methodol., which cannot be overcome by themselves, are pointed out. Also, a new algorithm of time scale is proposed by means of the dynamic model of atomic clock, and the simulation on computer is carried out.

=> => d stat que l98 nos
L66 STR
L68 601 SEA FILE=REGISTRY SSS FUL L66
L69 STR
L70 12 SEA FILE=REGISTRY SUB=L68 SSS FUL L69
L71 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L70
L72 589 SEA FILE=REGISTRY ABB=ON PLU=ON L68 NOT L70
L73 102 SEA FILE=HCAPLUS ABB=ON PLU=ON L72
L74 86 SEA FILE=HCAPLUS ABB=ON PLU=ON L73 AND PD=<OCTOBER 24, 2003
L75 86 SEA FILE=HCAPLUS ABB=ON PLU=ON L74 NOT L71
L76 20 SEA FILE=HCAPLUS ABB=ON PLU=ON L75 AND PATENT/DT
L77 66 SEA FILE=HCAPLUS ABB=ON PLU=ON L75 NOT L76
L79 19 SEA FILE=HCAPLUS ABB=ON PLU=ON ("DUNNING L"/AU OR "DUNNING L A"/AU OR "DUNNING L K"/AU OR "DUNNING L KAY"/AU OR "DUNNING L L"/AU OR "DUNNING L M"/AU OR "DUNNING LAURA"/AU)
L80 18 SEA FILE=HCAPLUS ABB=ON PLU=ON L79 NOT (L71 OR L76 OR L77)
L81 38 SEA FILE=HCAPLUS ABB=ON PLU=ON ("JAROCH S"/AU OR "JAROCH STEFAN"/AU)
L82 37 SEA FILE=HCAPLUS ABB=ON PLU=ON L81 NOT (L71 OR L76 OR L77 OR L80)
L83 32 SEA FILE=HCAPLUS ABB=ON PLU=ON ("KOCHANNY M"/AU OR "KOCHANNY MONICA"/AU OR "KOCHANNY MONICA J"/AU OR "KOCHANNY MONICA JEAN"/AU)
L84 31 SEA FILE=HCAPLUS ABB=ON PLU=ON L83 NOT (L71 OR L76 OR L77 OR L80 OR L82)
L87 118 SEA FILE=HCAPLUS ABB=ON PLU=ON "LIANG M"/AU OR ("LIANG M L"/AU OR "LIANG M LI H"/AU) OR ("LIANG MEINA"/AU OR "LIANG MEINA L"/AU)
L88 111 SEA FILE=HCAPLUS ABB=ON PLU=ON L87 NOT (L71 OR L76 OR L77 OR L80 OR L82 OR L84)
L89 16 SEA FILE=HCAPLUS ABB=ON PLU=ON "LU SHOU FU"/AU
L91 22 SEA FILE=HCAPLUS ABB=ON PLU=ON ("ONUFFER J"/AU OR "ONUFFER J J"/AU OR "ONUFFER JAMES"/AU OR "ONUFFER JAMES J"/AU OR "ONUFFER JAMES JOSEPH"/AU)
L92 20 SEA FILE=HCAPLUS ABB=ON PLU=ON L91 NOT (L71 OR L76 OR L77 OR L80 OR L82 OR L84 OR L89)
L93 945 SEA FILE=HCAPLUS ABB=ON PLU=ON ("PHILLIPS G"/AU OR "PHILLIPS G A"/AU OR "PHILLIPS G B"/AU OR "PHILLIPS G B JR"/AU OR "PHILLIPS G BRIGGS"/AU OR "PHILLIPS G C"/AU OR "PHILLIPS G D"/AU OR "PHILLIPS G E"/AU OR "PHILLIPS G E S"/AU OR "PHILLIPS G F"/AU OR "PHILLIPS G FRANK"/AU OR "PHILLIPS G H"/AU OR "PHILLIPS G J"/AU OR "PHILLIPS G L"/AU OR "PHILLIPS G L II"/AU OR "PHILLIPS G M"/AU OR "PHILLIPS G N"/AU OR "PHILLIPS G N JR"/AU OR "PHILLIPS G N ONUOHA"/AU OR "PHILLIPS G NEIL"/AU OR

```
                "PHILLIPS G O"/AU OR "PHILLIPS G R"/AU OR "PHILLIPS G T"/AU OR
                "PHILLIPS G W"/AU OR "PHILLIPS G W M"/AU OR "PHILLIPS G W MAC
                PHERSON"/AU OR "PHILLIPS G W MACPHERSON"/AU) OR ("PHILLIPS
                GARY A"/AU OR "PHILLIPS GARY B"/AU OR "PHILLIPS GARY BRUCE"/AU
                OR "PHILLIPS GARY C"/AU OR "PHILLIPS GARY J"/AU OR "PHILLIPS
                GARY JOHN"/AU OR "PHILLIPS GARY M"/AU OR "PHILLIPS GARY S"/AU
                OR "PHILLIPS GARY W"/AU OR "PHILLIPS GARY WILSON"/AU)
L94          62 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "WEI GUO"/AU OR ("WEI GUO
                PIN"/AU OR "WEI GUO PING"/AU)
L95          56 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L94 NOT (L71 OR L76 OR L77 OR
                L80 OR L82 OR L84 OR L89 OR L92)
L96         142 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("YE BIN"/AU OR "YE BIN
                QI"/AU)
L97         131 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L96 NOT (L71 OR L76 OR L77 OR
                L80 OR L82 OR L84 OR L89 OR L92 OR L95)
L98           0 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L88 AND L93 AND L97


=>
=>

=> d stat que l99 nos l99
'L114' IS NOT VALID HERE

=> d stat que l99 nos
L66             STR
L68         601 SEA FILE=REGISTRY SSS FUL L66
L69             STR
L70          12 SEA FILE=REGISTRY SUB=L68 SSS FUL L69
L71           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L70
L72         589 SEA FILE=REGISTRY ABB=ON  PLU=ON  L68 NOT L70
L73         102 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L72
L74          86 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L73 AND PD=<OCTOBER 24, 2003
L75          86 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L74 NOT L71
L76          20 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L75 AND PATENT/DT
L77          66 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L75 NOT L76
L79          19 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("DUNNING L"/AU OR "DUNNING L
                A"/AU OR "DUNNING L K"/AU OR "DUNNING L KAY"/AU OR "DUNNING L
                L"/AU OR "DUNNING L M"/AU OR "DUNNING LAURA"/AU)
L80          18 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L79 NOT (L71 OR L76 OR L77)
L81          38 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("JAROCH S"/AU OR "JAROCH
                STEFAN"/AU)
L82          37 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L81 NOT (L71 OR L76 OR L77 OR
                L80)
L83          32 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("KOCHANNY M"/AU OR "KOCHANNY
                MONICA"/AU OR "KOCHANNY MONICA J"/AU OR "KOCHANNY MONICA
                JEAN"/AU)
L84          31 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L83 NOT (L71 OR L76 OR L77 OR
                L80 OR L82)
L87         118 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "LIANG M"/AU OR ("LIANG M
                L"/AU OR "LIANG M LI H"/AU) OR ("LIANG MEINA"/AU OR "LIANG
                MEINA L"/AU)
L88         111 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L87 NOT (L71 OR L76 OR L77 OR
                L80 OR L82 OR L84)
L89          16 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "LU SHOU FU"/AU
L91          22 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("ONUFFER J"/AU OR "ONUFFER J
                J"/AU OR "ONUFFER JAMES"/AU OR "ONUFFER JAMES J"/AU OR
                "ONUFFER JAMES JOSEPH"/AU)
L92          20 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L91 NOT (L71 OR L76 OR L77 OR
                L80 OR L82 OR L84 OR L89)
```

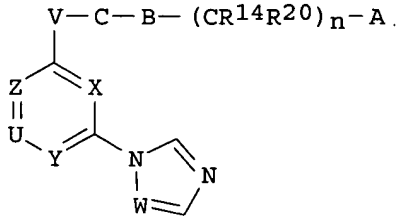
```
L93         945 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("PHILLIPS G"/AU OR "PHILLIPS
                G A"/AU OR "PHILLIPS G B"/AU OR "PHILLIPS G B JR"/AU OR
                "PHILLIPS G BRIGGS"/AU OR "PHILLIPS G C"/AU OR "PHILLIPS G
                D"/AU OR "PHILLIPS G E"/AU OR "PHILLIPS G E S"/AU OR "PHILLIPS
                G F"/AU OR "PHILLIPS G FRANK"/AU OR "PHILLIPS G H"/AU OR
                "PHILLIPS G J"/AU OR "PHILLIPS G L"/AU OR "PHILLIPS G L II"/AU
                OR "PHILLIPS G M"/AU OR "PHILLIPS G N"/AU OR "PHILLIPS G N
                JR"/AU OR "PHILLIPS G N ONUOHA"/AU OR "PHILLIPS G NEIL"/AU OR
                "PHILLIPS G O"/AU OR "PHILLIPS G R"/AU OR "PHILLIPS G T"/AU OR
                "PHILLIPS G W"/AU OR "PHILLIPS G W M"/AU OR "PHILLIPS G W MAC
                PHERSON"/AU OR "PHILLIPS G W MACPHERSON"/AU) OR ("PHILLIPS
                GARY A"/AU OR "PHILLIPS GARY B"/AU OR "PHILLIPS GARY BRUCE"/AU
                OR "PHILLIPS GARY C"/AU OR "PHILLIPS GARY J"/AU OR "PHILLIPS
                GARY JOHN"/AU OR "PHILLIPS GARY M"/AU OR "PHILLIPS GARY S"/AU
                OR "PHILLIPS GARY W"/AU OR "PHILLIPS GARY WILSON"/AU)
L94          62 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "WEI GUO"/AU OR ("WEI GUO
                PIN"/AU OR "WEI GUO PING"/AU)
L95          56 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L94 NOT (L71 OR L76 OR L77 OR
                L80 OR L82 OR L84 OR L89 OR L92)
L96         142 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("YE BIN"/AU OR "YE BIN
                QI"/AU)
L97         131 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L96 NOT (L71 OR L76 OR L77 OR
                L80 OR L82 OR L84 OR L89 OR L92 OR L95)
L99           0 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L88 AND (L93 OR L97)


=>
=>

=> d stat que l100 nos
L66             STR
L68         601 SEA FILE=REGISTRY SSS FUL L66
L69             STR
L70          12 SEA FILE=REGISTRY SUB=L68 SSS FUL L69
L71           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L70
L72         589 SEA FILE=REGISTRY ABB=ON  PLU=ON  L68 NOT L70
L73         102 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L72
L74          86 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L73 AND PD=<OCTOBER 24, 2003
L75          86 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L74 NOT L71
L76          20 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L75 AND PATENT/DT
L77          66 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L75 NOT L76
L79          19 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("DUNNING L"/AU OR "DUNNING L
                A"/AU OR "DUNNING L K"/AU OR "DUNNING L KAY"/AU OR "DUNNING L
                L"/AU OR "DUNNING L M"/AU OR "DUNNING LAURA"/AU)
L80          18 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L79 NOT (L71 OR L76 OR L77)
L81          38 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("JAROCH S"/AU OR "JAROCH
                STEFAN"/AU)
L82          37 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L81 NOT (L71 OR L76 OR L77 OR
                L80)
L83          32 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("KOCHANNY M"/AU OR "KOCHANNY
                MONICA"/AU OR "KOCHANNY MONICA J"/AU OR "KOCHANNY MONICA
                JEAN"/AU)
L84          31 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L83 NOT (L71 OR L76 OR L77 OR
                L80 OR L82)
L89          16 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "LU SHOU FU"/AU
L91          22 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("ONUFFER J"/AU OR "ONUFFER J
                J"/AU OR "ONUFFER JAMES"/AU OR "ONUFFER JAMES J"/AU OR
                "ONUFFER JAMES JOSEPH"/AU)
L92          20 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L91 NOT (L71 OR L76 OR L77 OR
                L80 OR L82 OR L84 OR L89)
```

```
L93          945 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("PHILLIPS G"/AU OR "PHILLIPS
                 G A"/AU OR "PHILLIPS G B"/AU OR "PHILLIPS G B JR"/AU OR
                 "PHILLIPS G BRIGGS"/AU OR "PHILLIPS G C"/AU OR "PHILLIPS G
                 D"/AU OR "PHILLIPS G E"/AU OR "PHILLIPS G E S"/AU OR "PHILLIPS
                 G F"/AU OR "PHILLIPS G FRANK"/AU OR "PHILLIPS G H"/AU OR
                 "PHILLIPS G J"/AU OR "PHILLIPS G L"/AU OR "PHILLIPS G L II"/AU
                 OR "PHILLIPS G M"/AU OR "PHILLIPS G N"/AU OR "PHILLIPS G N
                 JR"/AU OR "PHILLIPS G N ONUOHA"/AU OR "PHILLIPS G NEIL"/AU OR
                 "PHILLIPS G O"/AU OR "PHILLIPS G R"/AU OR "PHILLIPS G T"/AU OR
                 "PHILLIPS G W"/AU OR "PHILLIPS G W M"/AU OR "PHILLIPS G W MAC
                 PHERSON"/AU OR "PHILLIPS G W MACPHERSON"/AU) OR ("PHILLIPS
                 GARY A"/AU OR "PHILLIPS GARY B"/AU OR "PHILLIPS GARY BRUCE"/AU
                 OR "PHILLIPS GARY C"/AU OR "PHILLIPS GARY J"/AU OR "PHILLIPS
                 GARY JOHN"/AU OR "PHILLIPS GARY M"/AU OR "PHILLIPS GARY S"/AU
                 OR "PHILLIPS GARY W"/AU OR "PHILLIPS GARY WILSON"/AU)
L94           62 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "WEI GUO"/AU OR ("WEI GUO
                 PIN"/AU OR "WEI GUO PING"/AU)
L95           56 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L94 NOT (L71 OR L76 OR L77 OR
                 L80 OR L82 OR L84 OR L89 OR L92)
L96          142 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("YE BIN"/AU OR "YE BIN
                 QI"/AU)
L97          131 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L96 NOT (L71 OR L76 OR L77 OR
                 L80 OR L82 OR L84 OR L89 OR L92 OR L95)
L100           3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L93 AND L97


=> d ibib abs 1-3

L100 ANSWER 1 OF 3  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2002:610405  HCAPLUS
DOCUMENT NUMBER:          137:169534
TITLE:                    Preparation of imidazolyl pyrimidinamines as NOS
                          inhibitors
INVENTOR(S):              Arnaiz, Damian O.; Baldwin, John J.; Davey, David D.;
                          Devlin, James J.; Dolle, Roland Ellwood, III;
                          Erickson, Shawn David; McMillan, Kirk; Morrissey,
                          Michael M.; Ohlmeyer, Michael H. J.; Pan, Gonghua;
                          Paradkar, Vidyadhar Madhav; Parkinson, John;
                          Phillips, Gary B.; Ye, Bin; Zhao,
                          Zuchun
PATENT ASSIGNEE(S):       Berlex Laboratories, Inc., USA; Pharmacopeia, Inc.
SOURCE:                   U.S., 132 pp., Cont.-in-part of U.S. Ser. No. 25,124,
                          abandoned.
                          CODEN: USXXAM
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   3
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     US 6432947            B1    20020813    US 1999-383813          19990826
     CN 1100777            B     20030205    CN 1998-804281          19980219
     CA 2376355            AA    20010301    CA 2000-2376355         20000824
     WO 2001014371         A1    20010301    WO 2000-US23173         20000824
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
             HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
             LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
             SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
```

	YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,				
	DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,				
	CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR	2000014144	A	20020521	BR 2000-14144	20000824
EP	1206467	A1	20020522	EP 2000-959333	20000824
EP	1206467	B1	20031217		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				
	IE, SI, LT, LV, FI, RO, MK, CY, AL				
SI	20818	C	20020831	SI 2000-20040	20000824
EE	200200091	A	20030415	EE 2002-91	20000824
NZ	517411	A	20030926	NZ 2000-517411	20000824
AT	256681	E	20040115	AT 2000-959333	20000824
AU	769405	B2	20040129	AU 2000-70671	20000824
PT	1206467	T	20040531	PT 2000-959333	20000824
ES	2213599	T3	20040901	ES 2000-959333	20000824
ZA	2002001485	A	20030521	ZA 2002-1485	20020221
NO	2002000925	A	20020416	NO 2002-925	20020226
BG	106440	A	20021129	BG 2002-106440	20020226
LT	4982	B	20030127	LT 2002-28	20020315
LV	12887	B	20030120	LV 2002-50	20020326
US	2002165203	A1	20021107	US 2002-121886	20020412
US	6841673	B2	20050111		
US	2002183323	A1	20021205	US 2002-121659	20020412
US	6864263	B2	20050308		
US	2003004137	A1	20030102	US 2002-121379	20020412
US	6747031	B2	20040608		
US	2003027794	A1	20030206	US 2002-121758	20020412
US	6846829	B2	20050125		
US	2003060452	A1	20030327	US 2002-121212	20020412
US	6849739	B2	20050201		
US	2003069210	A1	20030410	US 2002-122072	20020412
US	6841674	B2	20050111		
US	2003073669	A1	20030417	US 2002-121682	20020412
US	2003078265	A1	20030424	US 2002-121808	20020412
US	6670473	B2	20031230		
US	2003083332	A1	20030501	US 2002-122047	20020412
US	6887865	B2	20050503		
US	2003092678	A1	20030515	US 2002-122006	20020412
US	6864368	B2	20050308		
PRIORITY APPLN. INFO.:				US 1997-808975	B2 19970219
				US 1998-25124	B2 19980217
				WO 1998-US3176	A 19980219
				US 1999-383813	A 19990826
				WO 2000-US23173	W 20000824

OTHER SOURCE(S): MARPAT 137:169534

GI



I

AB The title compds. [I; U = N, CR5 (R5 = H, halo, alkyl, optionally substituted aralkyl or aryl, etc.); V = NR4, S, O, CHR4 (R4 = H, alkyl, aryl, aralkyl, cycloalkyl); W = N, CH; X, Y, Z = N, CR19 (R19 = H, alkyl, cyclopropyl, halo, haloalkyl); A = R1, OR1, CONR1R2, PO(NR1R2)2, NR1COR2, etc. (R1, R2 = H, optionally substituted alkyl or cycloalkyl, etc. or NR1R2 = N-heterocyclyl); B = CR17(CHR15)mQR3 (m = 1-4, R3 = H, alkyl, cycloalkyl, optionally substituted aryl, etc.; R15, R17 = H, alkyl; Q = CO, O, C:NR1, etc.); C = (CHR12)q(CHR13)r (q, r = 0-1; R12, R13 = H, alkyl); or B = C = null; R14, R20 = H, alkyl; n = 1-3], useful as inhibitors of nitric oxide synthase, were prepared Thus, N-[(1,3-benzodioxol-5-yl)methyl]-1-[3-(1H-imidazol-1-yl)phenyl]piperidine-2-acetamide was prepared by reaction of 1-(3-aminophenyl)imidazole, Et 7-chloro-3-oxoheptanoate, and piperonylamine. All exemplified compds. I showed iNOS inhibitory activity at concns. less than 25 μM.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L100 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:152677 HCAPLUS

DOCUMENT NUMBER: 134:193443

TITLE: Preparation of N-(aminopyrimidinyl)heterocycles as NOS inhibitors

INVENTOR(S): Arnaiz, Damian O.; Baldwin, John J.; Davey, David D.; Devlin, James J.; Dolle, Roland Ellwood, III; Erickson, Shawn David; Mcmillan, Kirk; Morrissey, Michael M.; Ohlmeyer, Michael H. J.; Pan, Gonghua; Paradkar, Vidyadhar Madhav; Parkinson, John; **Phillips, Gary B.**; **Ye, Bin**; Zhao, Zuchun

PATENT ASSIGNEE(S): Berlex Laboratories, Inc., USA; Pharmacopeia, Inc.

SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

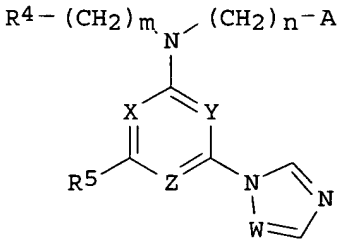
FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

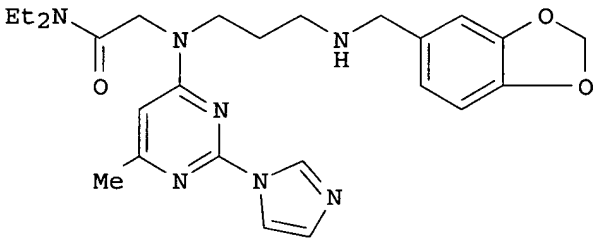
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001014371	A1	20010301	WO 2000-US23173	20000824
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6432947	B1	20020813	US 1999-383813	19990826
CA 2376355	AA	20010301	CA 2000-2376355	20000824
BR 2000014144	A	20020521	BR 2000-14144	20000824
EP 1206467	A1	20020522	EP 2000-959333	20000824
EP 1206467	B1	20031217		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
SI 20818	C	20020831	SI 2000-20040	20000824
EE 200200091	A	20030415	EE 2002-91	20000824
NZ 517411	A	20030926	NZ 2000-517411	20000824
AT 256681	E	20040115	AT 2000-959333	20000824

AU 769405	B2	20040129	AU 2000-70671		20000824
NO 2002000925	A	20020416	NO 2002-925		20020226
BG 106440	A	20021129	BG 2002-106440		20020226
PRIORITY APPLN. INFO.:			US 1999-383813	A1	19990826
			US 1997-808975	B2	19970219
			US 1998-25124	B2	19980217
			WO 2000-US23173	W	20000824

OTHER SOURCE(S): MARPAT 134:193443
GI



I



II

AB Title compds. (I) [wherein W = N or CH; 2 of X, Y, and Z = N and the other = CH; n and m = independently 1-4; A = CO2R1 or CONR1R2; R1 = independently H, (ar)alkyl, or aryl; R2 = independently H, alkyl, (CH2)nN(R1)2, (un)substituted heterocyclylalkyl or aralkyl; when m = 2-4, R4 can be OH, NR1R2, NR1COR1, NR1CO2R1, NR1S(O)tR1, or NR1CON(R1)2; when m = 1-4; R4 can also be CN or heterocyclyl; R5 = H, halo, (ar)alkyl, aryl, or haloalkyl; t = 0-2; and stereoisomers thereof] were prepared as inhibitors of nitric oxide synthase (NOS). For example, II was formed in a 5-step sequence involving (1) coupling N-cyanoethyl glycine Et ester with 4-chloro-6-methyl-2-methylsulfonylpyrimidine, (2) addition of imidazole to the pyrimidine, (3) deesterification using LiOH, (4) amidation with Et2NH, and (5) reductive addition of piperonal to the nitrile using Raney nickel and NaBH(OAc)3. I inhibited nitrogen oxide production in RAW 264.7 mouse monocyte cells and demonstrated the ability to treat the arthritis present in male Lewis rats (no specific data available for either assay). As NOS inhibitors, I are useful in the treatment of pathologies ascribed to abnormalities in nitrogen oxide production, e.g. multiple sclerosis, rheumatoid arthritis, dilated cardiomyopathy, and congestive heart failure.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L100 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:604917 HCAPLUS
DOCUMENT NUMBER: 129:231019

TITLE: Preparation of N-heterocyclic derivatives as NOS inhibitors

INVENTOR(S): Arnaiz, Damian O.; Baldwin, John J.; Davey, David D.; Devlin, James J.; Dolle, Roland Ellwood, III; Erickson, Shawn David; McMillan, Kirk; Morrissey, Michael M.; Ohlmeyer, Hichael H. J.; Pan, Gonghua; Paradkar, Vidyadhar Madhav; Parkinson, John; **Phillips, Gary B.**; **Ye, Bin**; Zhao, Zuchun; et al.

PATENT ASSIGNEE(S): Berlex Laboratories, Inc., USA; Pharmacopeia, Inc.; et al.

SOURCE: PCT Int. Appl., 358 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

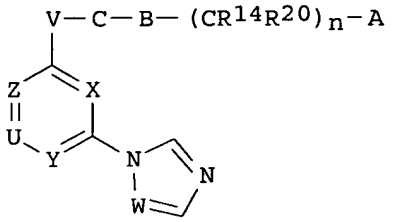
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9837079	A1	19980827	WO 1998-US3176	19980219
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2281545	AA	19980827	CA 1998-2281545	19980219
AU 9861749	A1	19980909	AU 1998-61749	19980219
AU 732969	B2	20010503		
EP 968206	A1	20000105	EP 1998-906555	19980219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
GB 2338957	A1	20000112	GB 1999-19686	19980219
NZ 337861	A	20010223	NZ 1998-337861	19980219
RU 2241708	C2	20041210	RU 1999-120077	19980219
NO 9903996	A	19991018	NO 1999-3996	19990819
HK 1025952	A1	20020412	HK 2000-104236	20000711
US 2003027794	A1	20030206	US 2002-121758	20020412
US 6846829	B2	20050125		
US 2003060452	A1	20030327	US 2002-121212	20020412
US 6849739	B2	20050201		
US 2003069210	A1	20030410	US 2002-122072	20020412
US 6841674	B2	20050111		

PRIORITY APPLN. INFO.:	US 1997-808975	A2	19970219
	US 1998-25124	A	19980217
	WO 1998-US3176	W	19980219
	US 1999-383813	A3	19990826

OTHER SOURCE(S): MARPAT 129:231019

GI



I

AB N-Heterocyclic derivs. I [U = N, CR5 (R5 = H, halo, alkyl, optionally substituted aralkyl or aryl, etc.); V = NR4, S, O, CHR4 (R4 = H, alkyl, aryl, aralkyl, cycloalkyl); W = N, CH; X, Y, Z = N, CR19 (R19 = H, alkyl, cyclopropyl, halo, haloalkyl); A = R1, OR1, CONR1R2, PO(NR1R2)2, NR1COR2, etc. (R1, R2 = H, optionally substituted alkyl or cycloalkyl, etc. or R1R2N = N-heterocyclyl); B = CR17(CHR15)mQR3 (m = 1-4, R3 = H, alkyl, cycloalkyl, optionally substituted aryl, etc.; R15, R17 = H, alkyl; Q = CO, O, C:NR1, etc.); N-heterocyclyl; C = (CHR12)q(CHR13)r (q, r = 0 or 1; R12, R13 = H, alkyl); or B = C = null; R14, R20 = H, alkyl; n = 1-3] were prepared as inhibitors of nitric oxide synthase. Thus, N-[(1,3-benzodioxol-5-yl)methyl]-1-[3-(1H-imidazol-1-yl)phenyl]piperidine-2-acetamide was prepared by reaction of 1-(3-aminophenyl)imidazole, 7-chloro-3-oxoheptanoic acid Et ester, and piperonylamine.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=>